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FILE LAST UPDATED: 18 Jul 2002 (20020718/ED)

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=> d all tot l114

L114 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:487374 HCAPLUS
DN 137:52399
TI Pharmaceutical **aerosol** formulations containing alkyl polyglycoside
IN Buckton, Graham; Columbano, Angela; Grosvenor, Martin; Wikeley, Philip
PA Astrazeneca Ab, Swed.
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
ICS A61K047-26
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002049616	A1	20020627	WO 2001-SE2853	20011219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI SE 2000-4750 A 20001219
AB The invention relates to a pharmaceutical **aerosol** formulation comprising a **surfactant** that is an alkyl polyglycoside (the av. degree of **polymn**. of 1-4) for the administration of a drug for inhalation. Propellant HFA-134a was was dispensed chilled (at

-55.degree.) into a 400-mL can. A valve was then crimped onto the can and the propellant allowed to return to ambient temp. **Beclomethasone dipropionate** was weighed into a 30-mL glass vial and 20 mL of **surfactant** (alkyl polyglycoside at 0.8 g/L) soln. in **water** . The resultant suspension was incubated at 25.degree. for 3 h hours, to allow adsorption of the **surfactant** to the **surface** of the drug, and to give a drug-**surfactant** ratio of 10 mg **surfactant**/g drug. The suspension was centrifuged and the **particles** of drug-**surfactant** were sepd. from the supernatant and dried in an oven at 50.degree. for 24 h. This was mixed with the propellant, and the final compn. contained **beclomethasone dipropionate** and glycoside 0.2% and HFA-134a to 100%.

ST pharmaceutical **aerosol** alkyl polyglycoside

IT Progestogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetals; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT **Drug delivery systems**
(**aerosols, inhalants**; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT **Drug delivery systems**
(**aerosols**; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT Glycosides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl polyglycosides; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT **Drug delivery systems**
(**microparticles**; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT Bronchodilators
Cholinergic antagonists
Propellants (sprays and foams)
Surfactants
(pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT Adrenoceptor agonists
(.beta.2-; pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

IT 431-89-0, HFA 227ea 811-97-2, HFA-134a **5534-09-8**, **Beclomethasone dipropionate** 23031-25-6, Terbutalin 51022-70-9, Salbutamol sulfate 51333-22-3, Budesonide 69227-93-6, n-Dodecyl .beta.-D-maltoside 73573-87-2, Formoterol 79794-75-5, Loratadine 89365-50-4, Salmeterol 90566-53-3, Fluticasone 105102-22-5, Mometasone 107753-78-6, Zafirlukast 144459-70-1, Rofleponide 150693-37-1, Symbicort 154189-36-3 154189-40-9 156410-05-8, Montanov 68 158966-92-8, Montelukast 186691-13-4, Tiotropium 189012-00-8 189012-09-7 201491-13-6, Berol Ag6202 208852-94-2, Glucopon 215CS 239797-88-7, Montanov 202 438576-82-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **aerosol** formulations contg. alkyl polyglycoside)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Astra Aktiebolag; WO 9619198 A1 1996 HCAPLUS
(2) Chuo Eazooru Kagaku Kk; JP 09-059606 A2 CAPLUS Accession No 1997:328726 1997 HCAPLUS
(3) Igen Inc; WO 0019980 A1 2000 HCAPLUS
(4) Minnesota Mining And Manufacturing Company; WO 9747286 A1 1997 HCAPLUS
(5) Minnesota Mining And Manufacturing Company; WO 9830244 A1 1998 HCAPLUS
(6) Uab Researchfoundation; WO 9500151 A1 1995 HCAPLUS

L114 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2002 ACS

AN **2002:428730** HCAPLUS
DN **137:10994**
TI Stabilizing biomolecules in liquid formulations
IN Cowan, Siu Man L.; McGinnis, Vincent; Palmer, Donna T.; Risser, Steven M.; Brody, Richard S.
PA Battelle Memorial Institute, USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC **63-6** (Pharmaceuticals)
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002043750	A2	20020606	WO 2001-US48834	20011030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-250491P P 20001201
AB The invention is directed to a stable formulation of a biol. active protein useful for **aerosol** delivery to the respiratory tract of a patient in need of treatment comprising: (a) a carrier liq. comprising from about 10 % to from about 100 % V/V water and from about 0 % to from about 90 % V/V of an org. liq.; (b) a biol. effective amt. of a protein suspended or dissolved in a carrier liq.; and (c) a stabilizing effective amt. of a derivatized carbohydrate stabilizing agent suspended or dissolved in said carrier liq. The stable formulations of the invention may optionally contain about 0.1 % to about 5.0 % wt./vol. of a pharmaceutically acceptable excipient. In an ethanol-water (80:20) carrier liq. the preferred stabilizer for insulin is C12-glucose, while in a totally aq. carrier liq. the preferred stabilizer is C8 glucose or C8 trehalose.
ST protein stabilizer liq formulation; carbohydrate stabilizer liq formulation biomol
IT **Drug delivery systems**
(**aerosols**; stabilizing biomols. in liq. formulations)
IT **Particle size**
Stabilizing agents
(stabilizing biomols. in liq. formulations)
IT Carbohydrates, biological studies
Glycosides
Perfluorocarbons
Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilizing biomols. in liq. formulations)
IT Antibodies
Antigens
Cytokines
Enzymes, biological studies
Hormones, animal, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilizing biomols. in liq. formulations)
IT 50-99-7, D-Glucose, biological studies 56-81-5, **Glycerol**, biological studies 57-50-1, **Sucrose**, biological studies

57-55-6, **Propylene glycol**, biological studies
59-23-4, D-Galactose, biological studies 64-17-5, Ethanol, biological studies 67-63-0, Isopropanol, biological studies 69-79-4, Maltose 71-36-3, 1-Butanol, biological studies 78-83-1, Isobutanol, biological studies 99-20-7, Trehalose **25322-68-3, Peg** 29836-26-8, Octyl .beta.-D-glucopyranoside 42939-93-5 59122-55-3, Dodecyl .beta.-D-glucopyranoside 64622-90-8
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilizing biomols. in liq. formulations)

IT 9001-27-8, Factor VIII 9004-10-8, Insulin, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilizing biomols. in liq. formulations)

IT 7732-18-5, Water, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilizing biomols. in liq. formulations)

L114 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:428681 HCAPLUS
DN 137:10984
TI Stable, **aerosolizable** suspensions of proteins in ethanol
IN Cowan, Siu Man L.
PA Batelle Memorial Institute, USA
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-00
CC **63-6** (Pharmaceuticals)
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002043695	A2	20020606	WO 2001-US48687	20011130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-250491P P 20001201

AB Stable suspensions of a biol. active protein are disclosed that are suited for **aerosol** delivery to the lungs of a patient in need of treatment, which comprise **particles** of biol. active protein suspended in ethanol. In a preferred embodiment, the invention describes a stable suspension of insulin useful for **aerosol** delivery to the lungs of a patient in need of treatment comprising **particles** of a pharmaceutically effective amt. of insulin suspended in ethanol. A method of delivering a therapeutically effective amt. of a protein to the respiratory tract of a patient is described which comprises producing an **aerosol** of a stable liq. suspension of a protein using an electrohydrodynamic spraying means wherein the liq. suspension comprises **particles** of the protein suspended in ethanol. The stable ethanol suspensions of the invention may optionally contain up to about 20% (vol./vol.) of a pharmaceutically acceptable formulation additive such as **glycerol, propylene glycol** and **polyethylene glycol** as well as minor amts. (about 0.05-5.0% wt./vol.) of a pharmaceutically acceptable excipient.

ST protein ethanol suspension **aerosol**

IT **Drug delivery systems**

(**aerosols**; prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT Spraying
(electrospraying; prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT Human
(prepn. of stable, **aerosolizable** suspensions of human proteins in ethanol)
IT **Particle size**
(prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT Antibodies
Antigens
Cytokines
Enzymes, biological studies
Hormones, animal, biological studies
Polyoxyalkylenes, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT Drug delivery systems
(suspensions; prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT 9004-10-8, Insulin, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)
IT 56-81-5, **Glycerol**, biological studies 57-55-6, **Propylene glycol**, biological studies 64-17-5, Ethanol, biological studies 9003-98-9, Deoxyribonuclease I **25322-68-3**, **Polyethylene glycol** 113189-02-9, Antihemophilic factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of stable, **aerosolizable** suspensions of proteins in ethanol)

L114 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:788221 HCAPLUS
TI Enhanced pulmonary absorption following **aerosol** administration of mucoadhesive powder **microspheres**
AU Sakagami, Masahiro; Sakon, Kiyoyuki; Kinoshita, Wataru; Makino, Yuji
CS DDS Research Laboratories, TEIJIN Ltd., Asahigaoka, Hino, Tokyo, 191-8512, Japan
SO J. Controlled Release (2001), 77(1-2), 117-129
CODEN: JCREEC; ISSN: 0168-3659
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC **63** (Pharmaceuticals)
AB Mucoadhesive, **hydroxypropylcellulose** (HPC) **microspheres** were prepd. for powder inhalation and their feasibility for enhancing pulmonary drug absorption was investigated. Respirable-sized **microspheres**, incorporating **cryst**. or amorphous fluorescein (used as a model drug), were prepd. by spray-drying aq. or **ethanol** HPC systems, resp. These were prepd. from a variety of HPC grades (SL, L, M and H types) in different fluorescein-HPC ratios (1:1-1:10). The **microspheres** were administered to tracheally-intubated guinea pigs as powder **aerosols** and their fluorescein pharmacokinetics studied, and compared to those for pure **cryst**. fluorescein ('control'). All **microspheres** were prepd. and **aerosolized** within a MMAD range of 1.3-2.6 .mu.m (GSD.ltoreq.2.1). Fluorescein's dissoln. was increased in the amorphous

form by 6.5-fold when compared to the **cryst**. material (83.9-87.2 vs. 13.5 .mu.g/mL, resp.). Poor dissoln. for the 'control' **cryst** . fluorescein appeared to be rate-detd., which showed bi-phasic absorption profiles (Tmax=60 min), simultaneously competing with mucociliary clearance out of the lower airways. While the **cryst**./HPC **microspheres** prolonged absorption, the amorphous fluorescein/HPC **microspheres** showed rapid absorption with Tmax=0 min (immediately after the administration had terminated). This was explained by enhanced fluorescein dissoln. and was consistently obsd. irresp. of the fluorescein-HPC ratio or HPC grade. However, the **microspheres** with the least viscous HPC-SL and the lowest fluorescein-HPC ratio (1:1) failed to enhance bioavailability, presumably because the mucociliary clearance was undisturbed. In contrast, the **microspheres** with the highly viscous HPC-H with ratios .gtoreq.1:4 successfully enhanced absorption, achieving 88.0% bioavailability by virtue of HPC increasing the dissoln. and retarding the mucociliary clearance.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Boobis, A; Respir Med 1998, V92(Suppl), P2
(2) Bot, A; Pharm Res 2000, V17, P275 HCAPLUS
(3) Brain, J; Aerosols in Medicine, Principle, Diagnosis and Therapy 1993, P117
(4) Brogden, R; Drugs 1975, V10, P166 MEDLINE
(5) Brogden, R; Drugs 1984, V28, P99 HCAPLUS
(6) Byron, P; J Pharm Sci 1986, V75, P168 HCAPLUS
(7) Byron, P; J Pharm Sci 1986, V75, P433 HCAPLUS
(8) Byron, P; Respiratory Drug Delivery 1990, P107 HCAPLUS
(9) Byron, P; Respiratory Drug Delivery 1990, P167 HCAPLUS
(10) Byron, P; Respiratory Drug Delivery 2000, V7, P41
(11) Chowhan, Z; J Pharm Sci 1976, V65, P1669 HCAPLUS
(12) Clark, A; J Pharm Sci 1985, V74, P939 HCAPLUS
(13) Colthorpe, P; Pharm Res 1992, V9, P746
(14) Cramer, P; Aerosols in Medicine, Principle, Diagnosis and Therapy 1993, P247
(15) Dolovich, M; J Aerosol Med 1999, V12(Suppl 1), PS9
(16) Edwards, D; Science 1997, V276, P1868 HCAPLUS
(17) El-Hameed, M; Int J Pharm 1999, V180, P59
(18) Gheber, L; Cell Motil Cytoskeleton 1998, V39, P9 MEDLINE
(19) Gonda, I; J Pharm Sci 1988, V77, P340 HCAPLUS
(20) Green, G; Arch Intern Med 1981, V131, P109
(21) Gupta, P; J Contolled Release 1988, V17, P129
(22) Hochhaus, G; Respiratory Drug Delivery 1996, V6, P45
(23) Illum, L; Pharm Res 1994, V11, P1186 HCAPLUS
(24) King, M; Biorheology 1993, V30, P49 MEDLINE
(25) Kumar, V; Drug Dev Ind Pharm 1993, V19, P1 HCAPLUS
(26) Lansley, A; Adv Drug Deliv Rev 1993, V11, P299 HCAPLUS
(27) Lee, J; J Pharm Sci 2000, V89, P850 HCAPLUS
(28) Morimoto, K; J Pharm Pharmacol 2000, V52, P611 HCAPLUS
(29) Nagai, T; Bioadhesive Drug Delivery Systems 1990, P169
(30) Okuda, M; Rhinology 1986, V24, P113 MEDLINE
(31) Patton, J; Adv Drug Deliv Rev 1996, V19, P3 HCAPLUS
(32) Pillai, R; J Appl Physiol 1998, V84, P717 MEDLINE
(33) Prime, D; Adv Drug Deliv Rev 1997, V26, P51 HCAPLUS
(34) Qui, Y; Int J Pharm 1995, V115, P95
(35) Taylor, G; Respiratory Drug Delivery 1994, V4, P25
(36) Warheit, D; Toxicology 1989, V20, P1 HCAPLUS

L114 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2002 ACS

AN **2001:257971** HCAPLUS

DN **134:271281**

TI Process for the preparation of aqueous dispersions of **particles** of **water-soluble polymers** and the **particles** obtained

IN Vanderhoff, John W.; Lu, Cheng Xun; Lee, Clarence C.; Tsai, Chi-Chun

PA C. R. Bard, Inc., USA; Lehigh University
SO U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 659,770, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K009-10
ICS A61K047-36; A61L027-52
NCL 424078170
CC **63-6** (Pharmaceuticals)
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6214331	B1	20010410	US 1997-989888	19971212 <--
WO 9931167	A1	19990624	WO 1998-US26094	19981209

W: IN, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1995-466676 B2 19950606 <--
US 1996-659770 B2 19960606
US 1997-989888 A 19971212

AB The invention is a process for the prepn. of crosslinked **water**-swellable **polymer particles**. First, an aq. **polymer** soln. contg. a **water-sol. polymer** having at least one functional group or charge, is combined with aq. medium. The aq. **polymer** soln. is then mixed under moderate agitation with an oil medium and an emulsifier to form an emulsion of **droplets** of the **water-sol. polymer**. A crosslinking agent capable of crosslinking the functional groups and/or charges in the **water-sol. polymer** is then added to the emulsion to form crosslinked **water**-swellable **polymer particles**. The invention also includes the **particles** formed by the process and aq. dispersions contg. the **particles** which are useful for administering to an individual. The **particles** of the invention are useful for implantation, soft tissue augmentation, and scaffolding to promote cell growth. A compn. for prepn. of crosslinked **water-sol particle** comprised **water** 100, Na alginate 7, NH4OH to pH 10-11 18 drops, Span 60 1, XAMA-7 crosslinking agent 4, and isopropanol 100 parts by wt.

ST **polymer water sol particle; microsphere polymer water sol particle;** implant **polymer water sol particle**

IT Glycoproteins, specific or class
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(emulsans; prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)

IT Prosthetic materials and Prosthetics
(implants; prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)

IT **Drug delivery systems**
(**microspheres**; prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)

IT Animal tissue culture
Crosslinking agents
Particle size
Particles
(prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants,

or scaffolds for cell growth)
IT Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)
IT Albumins, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(serum; prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)
IT Globulins, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.gamma.-; prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)
IT 51834-17-4, Hexadecyl sodium phthalate
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)
IT 1338-41-6, **Sorbitan** monostearate 1398-61-4, Chitin 9000-07-1, Carrageenan 9002-89-5 9003-39-8, **Pvp** 9004-54-0, **Dextran**, biological studies 9004-61-9, Hyaluronic acid 9004-67-5, Methyl **cellulose** 9005-25-8, Starch, biological studies 9005-38-3, Sodium alginate 9005-79-2, Glycogen, biological studies 9005-82-7, Amylose 9007-28-7, Chondroitin sulfate 9012-36-6, Agarose 9012-76-4, Chitosan 9037-22-3, Amylopectin 11138-66-2, Xanthan 24967-94-0, Dermatan sulfate **25322-68-3**, **Peg** 54724-00-4, Curdlan 71010-52-1, Gellan gum 169799-44-4, Keratin sulfate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prepn. of aq. dispersions of **particles** of **water-sol. polymers** for **microspheres**, implants, or scaffolds for cell growth)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 9639464 1996 HCAPLUS
(2) Berg; US 5007940 1991
(3) Soon-Siong, P; US 5705270 1998 HCAPLUS
(4) Tanihara; US 5770229 1998 HCAPLUS
(5) Thompson; US 5684051 1997 HCAPLUS

L114 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:706335 HCAPLUS
DN 133:271748
TI Compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compositions of powder **aerosols**
IN Diederichs, Julia Eva; Koch, Wolfgang; Loedding, Hubert; Reszka, Regina; Windt, Horst
PA Max-Delbrueck-Centrum fuer Molekulare Medizin, Germany; Fraunhofer-Gesellschaft zur Foerderung der Angewandten Forschung e.V.
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent

LA German
IC ICM A61M015-00
ICS A61K009-127; A61K009-51
CC **63-7** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10004860	A1	20001005	DE 2000-10004860	20000203
	EP 1148905	A2	20011031	EP 2000-912355	20000203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	DE 1999-19905285	A1	19990203		
	DE 1999-19954107	A1	19991102		
	WO 2000-DE337	W	20000203		

AB The invention concerns an **inhaler** for the delivery of lung disease drugs in the form of liposomal powders from an aq. soln. comprizing a container for the soln., a **nebulizer**, compressed air to avoid strenuous inhaling, a spray drying unit and a mouth piece. The sprayed **aerosol** powder is dry, does not contain cryoprotectors, the **particles** are **spheric** and have amorphous or cryst. structure and their size is 0.5-10 .mu.m. The powder **aerosol** is composed of liposomes and/or **nanoparticles**. The compn. contains phospholipids, **cholesterol**, pulmonary **surfactants** or cationic amphiphiles, and the drug. The liposome powder liposomes are multilamellar vesicles (MLV) or small unilamellar vesicles (SUV). **Nanoparticles** are either the drug components or **polymers** that carry the drugs. Liposomes and **nanoparticles** can be **surface**-modified; modifiers are **PEG**, plasma proteins, **surfactant**-assocd. proteins, antibodies. furthermore the subject of the invention is consisting a new powder **aerosol**, of Liposomen or nano-**particles**.

ST **inhaler** liposome powder **aerosol** drug dosing lung compressed air

IT Amphiphiles
(cationic; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

IT Bronchi
Drug delivery systems
Lung, disease
Particle size
Pulmonary **surfactant**
Spray atomizers
Trachea (anatomical)
(compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

IT **Gelatins**, biological studies
Polyesters, biological studies
Polyoxyalkylenes, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

IT Air
(compressed; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

IT **Drug delivery systems**
(**inhalants**; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

IT **Medical goods**
(**inhalers**; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT **Drug delivery systems**
(liposomes; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT Liposomes
(multilamellar; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT Liposomes
(small unilamellar; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT Phosphatidylcholines, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(soya; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT **Drug delivery systems**
(**sprays**; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT Proteins, general, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**surfactant**-modified; compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)
IT 57-88-5, **Cholesterol**, biological studies 2462-63-7, 9-Octadecenoic acid (9Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester 9003-20-7, **Polyvinylacetate** 9003-39-8, **Polyvinylpyrrolidone** 9005-32-7, Alginic acid 9011-14-7, **Polymethylmethacrylate 25322-68-3**, **PEG** 26100-51-6, Lactic acid **homopolymer** 137056-72-5
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compressed air **inhaler** device for dosing liposome powder **aerosol** in treating lung diseases and compns. of powder **aerosols**)

L114 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:335216 HCAPLUS
DN 132:339372
TI **Aerosols** comprising **nanoparticle** drugs
IN **Bosch, H. William**; Ostrander, Kevin D.; Cooper, Eugene R.
PA Nanosystems, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-14
ICS A61K009-72
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000027363	A1	20000518	WO 1999-US26799	19991112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,

JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1128814 A1 20010905 EP 1999-956981 19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI US 1998-190138 A 19981112
WO 1999-US26799 W 19991112

AB The invention discloses aq. dispersions of **nanoparticulate aerosol** formulations, dry powder **nanoparticulate aerosol** formulation, propellant-based **aerosol** formulations, methods of using the formulations in **aerosol** delivery devices, and methods of making such formulations. The **nanoparticles** of the aq. dispersions or dry powder formulations comprise insol. drug **particles** having a **surface** modifier on the **surface** thereof. An examples was given to demonstrate the ability to **aerosolize** a concd. **nanoparticulate** dispersion in an ultrasonic **nebulizer** which incorporates a fine mesh screen in its design. An addnl. purpose was to demonstrate that a therapeutic quantity of a concd. **nanoparticulate corticosteroid** (**beclomethasone dipropionate**) can be **aerosolized** in a very short time, e.g., <2 s.

ST **aerosol nanoparticle** drug

IT **Particle size**
Spray atomizers
(**aerosols** comprising **nanoparticle** drugs)

IT **Corticosteroids**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**aerosols** comprising **nanoparticle** drugs)

IT **Drug delivery systems**
(**aerosols**; **aerosols** comprising **nanoparticle** drugs)

IT **Drug delivery systems**
(**inhalants**; **aerosols** comprising **nanoparticle** drugs)

IT **Medical goods**
(**inhalers**; **aerosols** comprising **nanoparticle** drugs)

IT **Drug delivery systems**
(**nanoparticles**; **aerosols** comprising **nanoparticle** drugs)

IT 50-99-7, Dextrose, biological studies 69-65-8, Mannitol
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**aerosols** comprising **nanoparticle** drugs)

IT 76-25-5, Triamcinolone acetonide **5534-09-8**, **Beclomethasone dipropionate** 22204-53-1, Naproxen
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**aerosols** comprising **nanoparticle** drugs)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Abbott Laboratories; WO 9527475 A 1995 HCAPLUS
(2) Eickhoff; US 5518738 A 1996 HCAPLUS
(3) Nanosystems L L C; WO 9625918 A 1996 HCAPLUS
(4) Nanosystems Llc; WO 9835666 A 1998 HCAPLUS
(5) Rtp Pharma Inc; WO 9938493 A 1999 HCAPLUS

L114 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:13914 HCAPLUS
DN 132:313515
TI An in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**
AU Ostrander, Kevin D.; **Bosch, H. William**; Bondanza, Donna M.
CS Division of Elan Pharmaceutical Technologies, King of Prussia, PA, 19406, USA
SO European Journal of Pharmaceutics and Biopharmaceutics (1999), 48(3), 207-215
CODEN: EJPBEL; ISSN: 0939-6411
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
Section cross-reference(s): 2
AB Short duration ultrasonic **nebulization** of a concd. NanoCrystal colloidal dispersion of **beclomethasone dipropionate** demonstrated an increased respirable fraction and decreased throat deposition when evaluated in an Andersen 8-stage cascade impactor in comparison to the com. available propellant-based product Vanceril. An aq.-based 1.25% wt./wt. colloidal dispersion of **beclomethasone dipropionate** when **aerosolized** via an Omron NE-U03 ultrasonic **nebulizer** generated a respirable drug dose from 22.6 to 39.4 .mu.g per 2 s actuation period, compared to 12.8 .mu.g for a single actuation of Vanceril. When viewed as a percentage of the emitted dose (through the actuator or mouthpiece), the respirable fraction ranged from 56 to 72% for the nanocryst. formulation vs. 36% for the propellant system. In addn., the throat deposition as seen in the induction port was 9-10% of the emitted dose for the novel suspension, as compared to 53% for the com. product. Thus, when used with the device outlined herein, a nanocryst. colloidal suspension of **beclomethasone dipropionate** affords greater potential drug delivery to the conductive airways of the lung in both quantity and as a percent of emitted dose. Addnl., lower potential throat deposition values were obsd. which may retard the development of undesirable side effects, such as candidiasis, when compared to a propellant based delivery system. Lastly, the ability to atomize aq.-based nanocryst. colloidal dispersions represents an environmentally sound alternative to the current chlorofluorocarbon (CFC)-based products and may avoid the tech. difficulties of reformulating with chlorine-free propellants.
ST NanoCrystal **beclomethasone dipropionate** delivery ultrasonic **nebulization**
IT Lung
Pharynx
(delivery; in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)
IT Anti-inflammatory agents
Antiasthmatics
Drug delivery systems
Particle size distribution
(in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)
IT **Corticosteroids**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)

IT **Drug delivery systems**
(**nanoparticles**; in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)
IT **Spray atomizers**
(ultrasonic; in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)
IT **5534-09-8, Beclomethasone dipropionate**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in-vitro assessment of a NanoCrystal **beclomethasone dipropionate** colloidal dispersion via ultrasonic **nebulization**)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; F-D-C Reports pink sheets 1998, 60 No 39, P14
(2) Anon; PDRR Electronic Library 1998
(3) Anon; Physician's Desk ReferenceR, 48th ed 1994
(4) Anon; United States Pharmacopeia 1995, P1761
(5) Berg, E; J Aerosol Sci 1988, V19, P1093 HCAPLUS
(6) Busse, W; World Asthma Meeting 1998
(7) Childers, A; Curr Therapeut Res 1996, V57, P75
(8) Dalby, R; Pharmaceut Technol March 1990, P27
(9) Harper, T; Am J Dis Child March 1981, V135, P219
(10) Key Pharmaceuticals; Package insert for VancerilR Inhaler 1993
(11) Leach, C; World Asthma Meeting 1998
(12) Leeds and Northrup; UPA150 Particle size analyzer operation and maintenance manual 1996
(13) Omron Healthcare, Inc; Omron model NE-U03 Instruction manual
(14) Susan, L; Pharm Develop Technol 1996, V3, P261
(15) Thompson, D; Pharmaceutical Inhalation Aerosol Technology 1992, P45
(16) Wiedman, T; Pharm Res 1997, V14, P112

L114 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:708592 HCAPLUS
DN 131:314233
TI **Aerosol** formulations of salmeterol xinafoate
IN Cooper, Simon Murray
PA Glaxo Group Ltd., UK
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-135
ICS A61K009-14; A61K009-12
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9955319	A1	19991104	WO 1999-EP2748	19990423
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9938213	A1	19991116	AU 1999-38213	19990423
	EP 1073429	A1	20010207	EP 1999-920757	19990423

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002512952 T2 20020508 JP 2000-545518 19990423

PRAI GB 1998-8802 A 19980424

WO 1999-EP2748 W 19990423

AB The present invention relates to formulations comprising **particulate** products which may be prepd. by methods and app. using supercrit. fluids. More particularly, the invention relates to formulations comprising certain cryst. forms of 4-hydroxy-.alpha.1-[[[6-(4-phenylbutoxy)hexyl]amino]methyl]-1,3-benzenedimethanol (salmeterol) 1-hydroxy-2-naphthalenecarboxylate (xinafoate). Accordingly, the present invention provides an **aerosol** pharmaceutical formulation comprising salmeterol xinafoate with a controlled **particle** size, shape and morphol., and a fluorocarbon, hydrogen-contg. fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant. E.g., the **inhalers** (25 .mu.g, 120 actuations) were prepd. by depositing 6.4 mg drug with controlled cryst. properties prepd. by using supercrit. CO2 into an 8 mL Presspart aluminum can. The can was closed by crimping on a Valois DF60 63 .mu.L valve before pressure-filling the canister with 12 g of propellant HFA 134a. The performance of the MDIs was measured based on drug deposition on the valve and actuator, and dose delivered through use. Total, interior, and exterior valve drug depositions from metered dose **inhalers** contg. conventionally crystd. (micronized) salmeterol xinafoate were 0.34, 012, and 0.22 mg compared to 0.13, 0.05, and 0.08 mg for drug prepd. by using supercrit. fluids.

ST salmeterol xinafoate crystal size morphol **inhaler**; **aerosol inhaler** salmeterol xinafoate chlorofluorocarbon fluorocarbon

IT Antiasthmatics

Crystal morphology

Particle size

Polymorphism (crystal)

(**aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT **Drug delivery systems**

(**aerosols, inhalants; aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT Hydrocarbons, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chlorofluorocarbons; **aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT Respiratory tract

(disease; **aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT Hydrocarbons, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fluoro; **aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT Extraction

(supercrit.; **aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT **5534-09-8, Beclomethasone dipropionate** 15826-37-6, Sodium cromoglycate 80474-14-2, Fluticasone propionate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**aerosol** formulations contg. salmeterol xinafoate with controlled cryst. properties)

IT 94749-08-3P, Salmeterol xinafoate

RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)

IT 811-97-2, HFA 134a

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**aerosol** formulations of salmeterol xinafoate with controlled cryst. properties)
IT 7631-86-9, **Silica**, properties
RL: PRP (Properties)
(deposition of salmeterol xinafoate with controlled cryst. properties from supercrit. carbon dioxide on fumed **silica**)
IT 124-38-9, Carbon dioxide, properties
RL: PRP (Properties)
(prepn. of salmeterol xinafoate with controlled cryst. properties for **aerosols** using supercrit. carbon dioxide)
IT 9004-64-2, Hydroxypropyl **cellulose**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of salmeterol xinafoate with controlled cryst. properties in **polymer** matrix using supercrit. fluid method for **aerosols**)
IT 69-72-7, processes
RL: REM (Removal or disposal); PROC (Process)
(purifn. of salmeterol xinafoate with controlled cryst. properties from impurities using supercrit. fluid method)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Glaxo Group Ltd; WO 9311745 A 1993 HCAPLUS
(2) Glaxo Group Ltd; WO 9501324 A 1995 HCAPLUS
(3) Sievers Robert E; WO 9317665 A 1993 HCAPLUS

L114 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:690935 HCAPLUS
DN 131:303393
TI Pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**
IN Cavaillon, Pascal; Llorca, Nathalie; Louis, Olivier; Rosier, Patrick
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
ICS A61K009-16; A61K031-57
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9953901	A1	19991028	WO 1999-EP2535	19990415
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2328882	AA	19991028	CA 1999-2328882	19990415
	AU 9935231	A1	19991108	AU 1999-35231	19990415
	BR 9909736	A	20001219	BR 1999-9736	19990415
	EP 1073417	A1	20010207	EP 1999-916921	19990415
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002512183	T2	20020423	JP 2000-544308	19990415
	NO 2000005218	A	20001110	NO 2000-5218	20001017
PRAI	GB 1998-8152	A	19980418		
	GB 1998-14709	A	19980708		
	WO 1999-EP2535	W	19990415		

AB The present invention relates to novel pharmaceutical **aerosol** formulations comprising: (A) a therapeutic agent in the form of **particles** coated by at least one coating excipient and at least one **surfactant**, in suspension in (B) a liquefied propellant gas for the administration of therapeutic agents particularly by the pulmonary route and to a process for prepg. these formulations. It also relates to novel **particles** suitable for use in such formulations. A suspension of **beclomethasone dipropionate** monohydrate 5, **lecithin** 0.5, and lactose 0.5% was spray-dried at 160.degree.. The spray-dried material was micronized. At least 90% of the **particle surface** was covered by coating layer after micronization. The **particles** were filed in cartridges and the finished product was stable for several month at room temp.

ST pharmaceutical **aerosol** coating therapeutic propellant **surfactant**

IT Perfluorocarbons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C1-4; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT **Surfactants**
(anionic; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT **Surfactants**
(cationic; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT Hydrocarbons, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorofluorocarbons, C1-4; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT Hydrocarbons, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoro, C1-4; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT **Surfactants**
(nonionic; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT **Particle size**
Propellants (sprays and foams)
Stability
Surfactants
(pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT Corn oil
Cottonseed oil
Disaccharides
Lecithins
Monosaccharides
Olive oil
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Sunflower oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT Drying
(spray; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)

IT **Drug delivery systems**
(**sprays**; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vegetable; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)
IT 9004-34-6, **Cellulose**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**microcryst.**; pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)
IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 99-20-7, Trehalose 110-27-0, Isopropyl myristate 111-62-6, Ethyl oleate 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 112-92-5, Stearyl alcohol 123-03-5, Cetyl pyridinium chloride 811-97-2, 1,1,1,2 Tetrafluoroethane 1323-38-2, Glyceryl monoricinoleate 1338-39-2, **Sorbitan** monolaurate 1338-43-8, **Sorbitan** monooleate 5420-17-7, Tetrahydrofurfuryl oleate 9002-92-0, Lauryl polyoxyethylene ether 9003-11-6, **Ethylene oxide propylene oxide copolymer** 9004-32-4, Carboxymethyl **cellulose** 9004-65-3, Methylhydroxypropyl **cellulose** 9004-98-2 9005-00-9, Stearyl polyoxyethylene ether 9005-65-6, Polyoxyethylene **sorbitan** monooleate 18559-94-9, Salbutamol 21209-30-3, **Diethylene glycol** dioleate **25322-68-3** 25496-72-4, Glyceryl monooleate 26266-58-0, **Sorbitan** trioleate 27215-38-9, Glyceryl monolaurate 31566-31-1, Glyceryl monostearate 36653-82-4, Cetyl alcohol **77011-63-3**, **Beclomethasone dipropionate** monohydrate 80474-14-2, Fluticasone propionate 89365-50-4, Salmeterol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **aerosol** formulation comprising coated therapeutic agents, propellants, and **surfactants**)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Glaxo Group Ltd; WO 9619968 A 1996 HCAPLUS
(2) Glaxo Group Ltd; WO 9736574 A 1997
(3) Hoechst Ag; EP 0655237 A 1995 HCAPLUS
(4) Inhale Therapeutic Systems Inc; WO 9829098 A 1998 HCAPLUS
(5) Innovata Biomed Ltd; EP 0257915 A 1988 HCAPLUS
(6) Leigh Steven; US 5141674 A 1992 HCAPLUS

L114 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:495156 HCAPLUS
DN 131:134647
TI **Microparticle** inhalation **aerosol** formulations containing phospholipids
IN Moussa, Iskandar; Parikh, Indu
PA RTP Pharma Inc., Can.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-00
ICS A61K009-14; A61K009-50; A61K009-51; A61K047-24; A61K047-06
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9938493	A1	19990805	WO 1998-US27922	19981230

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6086376	A	20000711	US 1998-16265	19980130	
CA 2319100	AA	19990805	CA 1998-2319100	19981230	
AU 9920244	A1	19990816	AU 1999-20244	19981230	
EP 1051154	A1	20001115	EP 1998-965051	19981230	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002501885	T2	20020122	JP 2000-529227	19981230	
SE 2000002643	A	20000904	SE 2000-2643	20000713	
PRAI US 1998-16265	A	19980130			
WO 1998-US27922	W	19981230			

AB **Aerosol** formulations contain stabilized **particles** of drug **microparticles** with a mean size range of 0.1-10 .mu. coated with a membrane-forming amphipathic lipid and dispersed in 1,1,1,2-tetrafluoroethane (HFA 134a) or 1,1,1,2,3,3,3-heptafluoropropane (HFA 227) propellant. Thus , an **aerosol microparticle** formulation contained **beclomethasone dipropionate** 0.0657, DPPC 0.0263, Myrj 52 0.0263, and HFA 134a 99.882.

ST **microparticle** inhalation **aerosol** phospholipid propellant

IT **Drug delivery systems**
(**aerosols, inhalants; microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT Density
Particle size distribution
Surfactants
(**microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT Perfluorocarbons
Phospholipids, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT **Drug delivery systems**
(**microparticles, aerosols; microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT Propellants (sprays and foams)
(propellants; **microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT Respiratory tract
(upper; **microparticle** inhalation **aerosol** formulations contg. phospholipids)

IT 76-25-5, Triamcinolone acetonide 431-89-0, HFA 227 811-97-2, HFA 134a 2644-64-6, 1,2-Dipalmitoylphosphatidylcholine 3385-03-3, Flunisolide **5534-09-8, Beclomethasone dipropionate** 9004-99-3, Myrj 52 18559-94-9, Salbutamol **25322-68-3** 61361-72-6, -Dimyristoylphosphatidylglycerol 106392-12-5, Poloxamer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**microparticle** inhalation **aerosol** formulations contg. phospholipids)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Andaris Ltd; WO 9744012 A 1997 HCAPLUS
(2) Andrew, S; WO 9618384 A 1996 HCAPLUS
(3) Boehringer Ingelheim Int; WO 9111495 A 1991 HCAPLUS
(4) Braun Melsungen Ag; EP 0535567 A 1993 HCAPLUS

(5) Byron, P; US 5492688 A 1996 HCAPLUS
(6) Glaxo Group Ltd; WO 9315741 A 1993 HCAPLUS
(7) Hoechst Ag; EP 0634166 A 1995 HCAPLUS
(8) Kjell, B; WO 9619197 A 1996 HCAPLUS
(9) Kjell, B; WO 9619198 A 1996 HCAPLUS
(10) Riker Laboratories Inc; WO 9104011 A 1991 HCAPLUS

L114 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:7794 HCAPLUS
DN 130:71555
TI Pharmaceutical **aerosol** composition comprising an active material, a propellant containing a hydrofluoroalkane and a cosolvent
IN Lewis, David; Ganderton, Davis; Meakin, Brian; Ventura, Paolo; Brambilla, Gaetano; Garzia, Raffaella
PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
ICS A61K009-72
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9856349	A1	19981217	WO 1998-EP3533	19980610
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	GB 2326334	A1	19981223	GB 1997-12434	19970613
	AU 9886262	A1	19981230	AU 1998-86262	19980610
	AU 729966	B2	20010215		
	EP 920302	A1	19990609	EP 1998-937474	19980610
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9805993	A	19990831	BR 1998-5993	19980610
	JP 2000516965	T2	20001219	JP 1999-501622	19980610
	EP 1219293	A2	20020703	EP 2002-7496	19980610
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, AL				
	ZA 9805136	A	19990107	ZA 1998-5136	19980612
	NO 9900594	A	19990413	NO 1999-594	19990209
	US 2001031244	A1	20011018	US 2001-796607	20010302
PRAI	GB 1997-12434	A	19970613		
	EP 1998-937474	A3	19980610		
	WO 1998-EP3533	W	19980610		
	US 1999-147669	A1	19990224		

AB A compn. for use in an **aerosol inhaler** comprises an active material, a propellant contg. a hydrofluoroalkane and a cosolvent. The compn. further includes a low volatility component which is added to increase the mass median aerodynamic diam. (MMAD) of the **aerosol particles** on actuation of the **inhaler**. With the addn. of the low volatility component, the MMAD of the **aerosol particles** may be comparable to the MMAD of **aerosol particles** of an **aerosol inhaler** including CFC as propellant. An **aerosol** contained **beclomethasone dipropionate** 50 mg/10mL, ethanol 14.9%, and HFA 134 a fill to 12 mL. The mean emitted dose was 222.1, MMAD 1.8, and fine **particle**

dose 67.4 .mu.g.
ST pharmaceutical **aerosol** propellant hydrofluoroalkane cosolvent; beclomethasone ethanol HFA 134a pharmaceutical **aerosol**
IT Solvents
(cosolvents; pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
IT Hydrocarbons, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoro; pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
IT **Particle size**
Propellants (fuels)
(pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
IT Alcohols, biological studies
Glycols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
IT **Drug delivery systems**
(**sprays**; pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
IT 64-17-5, Ethanol, biological studies 112-80-1, Oleic acid, biological studies 431-89-0, Hfa 227 811-97-2, HFA 134a 3385-03-3, Flunisolide **5534-09-8, Beclomethasone dipropionate** 18559-94-9, Salbutamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **aerosol** compn. comprising active material, propellant contg. hydrofluoroalkane and cosolvent)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ciba-Geigy AG; EP 0504112 A2 1992 HCAPLUS
(2) Dr Willmar Schwabe GMBH & Co; DE 4123663 A1 1993
(3) Glaxo Group Ltd; WO 92/08446 A1 1992 HCAPLUS
(4) Glaxo Group Ltd; WO 93/11745 A1 1993 HCAPLUS
(5) Hoechst Aktiengesellschaft; EP 0384371 A1 1990 HCAPLUS
(6) Jager, P; WO 94/13262 A1 1994 HCAPLUS
(7) Minnesota Mining and Manufacturing Company; WO 93/11747 A1 1993 HCAPLUS
(8) Riker Laboratories, Inc; EP 0372777 A2 1990 HCAPLUS
(9) Schering Corporation; EP 0518600 A1 1992 HCAPLUS
(10) Schering Corporation; EP 0518601 A1 1992 HCAPLUS

L114 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:13829 HCAPLUS
DN 128:79994
TI Medicinal **aerosol** formulations containing formoterol
IN Oliver, Martin J.; Paling, Simon G.; Jinks, Philip A.; Jaiswal, Sukhbinder K.
PA Minnesota Mining and Manufacturing Company, USA; Oliver, Martin J.; Paling, Simon G.; Jinks, Philip A.; Jaiswal, Sukhbinder K.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9747286	A1	19971218	WO 1997-US9471	19970602

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,

PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

	ZA 9704546	A	19981123	ZA 1997-4546	19970523
	CA 2257841	AA	19971218	CA 1997-2257841	19970602
	AU 9733739	A1	19980107	AU 1997-33739	19970602
	AU 726382	B2	20001102		
	EP 934057	A1	19990811	EP 1997-929756	19970602
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP 2000513340	T2	20001010	JP 1998-501656	19970602
	US 6054488	A	20000425	US 1998-88871	19980602
	NO 9805720	A	19990211	NO 1998-5720	19981207
PRAI	GB 1996-12297	A	19960611		
	US 1997-48233P	P	19970602		
	WO 1997-US9471	W	19970602		

AB A pharmaceutical suspension formulation suitable for **aerosol** administration having from 0.0025 to 0.1 wt./wt. of micronized formoterol (I), or an acid addn. salt thereof, from 0.1 to 5.0 wt./wt. **ethanol**, HFA 134a, HFA 227 or a mixt. of HFA 227 and HFA 134a, and optionally a **surfactant** other than a monoacetylated or diacetylated monoglyceride. The formulation being further characterized in that it exhibits substantially no growth in **particle** size or change in **crystal** morphol. of the drug over a prolonged period, is substantially and readily redispersible, and upon redispersion does not flocculate so quickly as to prevent reproducible dosing of the drug. An **aerosol** formulation contained I 0.010, **ethanol** 2.500, HFA-227 48.745, and HFA 134a 48.745%.

ST medicinal **aerosol** HFA 134a formoterol HFA227

IT **Particle size**
Propellants (sprays and foams)
Surfactants
Thickening agents
(medicinal **aerosol** formulations contg. formoterol)

IT **Drug delivery systems**
(**sprays**; medicinal **aerosol** formulations contg. formoterol)

IT 50-81-7, Ascorbic acid, biological studies 50-99-7, Glucose, biological studies 63-42-3, Lactose 64-17-5, **Ethanol**, biological studies 99-20-7 112-80-1, Oleic acid, biological studies 302-72-7, DL Alanine 431-89-0, HFA 227 811-97-2, HFA 134a 43229-80-7, Formoterol fumarate 73573-87-2, Formoterol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicinal **aerosol** formulations contg. formoterol)

L114 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:411227 HCAPLUS
DN 127:85999
TI Preparation and subsequent degradation of poly(L-lactic acid) **microspheres** suitable for **aerosolization**: a physicochemical study
AU El-Baseir, Mokhtar M.; Phipps, Mark A.; Kellaway, Ian W.
CS Welsh School Pharmacy, University Wales Cardiff, Cardiff, CF1 3XF, UK
SO International Journal of Pharmaceutics (1997), 151(2), 145-153
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier
DT Journal
LA English
CC **63-6** (Pharmaceuticals)
AB The **encapsulation** of nedocromil sodium and **beclomethasone dipropionate** with **microspheres** of poly(L-lactic acid) was studied and prepn. conditions optimized for

entrapment efficiency and **microsphere** size suitable for inhalation. DSC was ued to characterize the **microspheres** both in terms of drug/**polymer** interaction and influence of annealing conditions on the Tg and degree of crystallinity. The absence of mol. interaction was confirmed by FTIR. Incubation of the **microspheres** in phosphate buffer at 37.degree. for 8 days demonstrated no chem. degrdn. of the **polymer** as evidenced by IR spectral anal. and ests. of percentage crystallinity. **Surface** morphol. and internal structure were consistent with a homogeneous degrdn. pattern.

ST **aerosol** polylactate **microsphere** degrdn

IT Polyesters, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT **Drug delivery systems**
(**microspheres**; prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT Crystallinity
Encapsulation
Fusion enthalpy
Glass transition temperature
(prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT **Drug delivery systems**
(**sprays**; prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT **Polymer** morphology
(**surface**; prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT 26161-42-2 26811-96-1, Poly(L-lactic acid)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

IT **5534-09-8, Beclomethasone dipropionate**
9002-89-5, **PVA** 69049-74-7, Nedocromil sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and degrdn. of poly(lactic acid) **microspheres** for **aerosols**)

L114 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2002 ACS

AN **1997:111181** HCAPLUS

DN **126:122477**

TI Method for the manufacture of minimal volume **capsules** containing biological material

IN Lamberti, Francis

PA Neocrin Company, USA

SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K009-16
ICS A61K009-50; A61F002-02; A61L027-00; C12N005-00; C12N011-04; B01J013-04

CC **63-6** (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640071	A1	19961219	WO 1996-US5732	19960424 <--
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5827707	A	19981027	US 1995-484778	19950607 <--

CA 2223417 AA 19961219 CA 1996-2223417 19960424 <--
AU 9655732 A1 19961230 AU 1996-55732 19960424 <--
EP 831785 A1 19980401 EP 1996-913124 19960424 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1995-484778 19950607 <--
WO 1996-US5732 19960424

AB The present invention provides methods and a device for producing minimal vol. **capsules** contg. viable cells or cellular aggregates. The methods and device use a two-phase aq. emulsion system to form a dispersion of **liq.** **capsule**-forming materials in a continuous **liq.** phase to which is added a suspension of biol. material. Alternatively, the biol. material can be added to one or the other of the **liq.** phases. The compn. of this emulsion is adjusted to promote the thermodynamically-driven process for **particle** engulfment by the dispersed **droplets** of **liq.** **capsule**-forming materials. Subsequently, the **droplets** engulf the biol. material to form a **liq.** film surrounding the tissue and are converted to solid form, resulting in **encapsulation** of the biol. material in min. vol. **capsules** . A method for **encapsulation** of islets of Langerhans comprises (1) prepg. an emulsion comprising a continuous phase biocompatible aq. soln. contg. **polyethylene glycol**, a dispersed phase biocompatible aq. **polymeric** soln. contg. **dextran**, alginate and the islets, (2) allowing the dispersed phase of the emulsion to engulf the islets, and (3) gelling the alginate.

ST cell **encapsulation polymer** implant; Langerhans islet **PEG dextran** alginate **microcapsule**

IT Ovary
(cells, of Chinese hamster; manuf. of minimal vol. **capsules** contg. biol. materials)

IT Adrenal medulla
Parathyroid gland
(cells; manuf. of minimal vol. **capsules** contg. biol. materials)

IT Liver
(hepatocyte; manuf. of minimal vol. **capsules** contg. biol. materials)

IT **Drug delivery systems**
(implants, **microcapsules**; manuf. of minimal vol. **capsules** contg. biol. materials)

IT Pancreatic islet of Langerhans
(insulinoma, .beta.-cell; manuf. of minimal vol. **capsules** contg. biol. materials)

IT Leukemia
(lymphocytic, cells; manuf. of minimal vol. **capsules** contg. biol. materials)

IT Bacteria (Eubacteria)
Microorganism
Pancreatic islet of Langerhans
T cell (lymphocyte)
(manuf. of minimal vol. **capsules** contg. biol. materials)

IT Antigens
Blood-coagulation factors
Drugs
Enzymes, biological studies
Hormones, animal, biological studies
Oligonucleotides
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Proteins, general, biological studies
Retroviridae
Vitamins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manuf. of minimal vol. **capsules** contg. biol. materials)
IT Nerve
(neuroblast, cells; manuf. of minimal vol. **capsules** contg. biol. materials)
IT Fibroblast
(of foreskin; manuf. of minimal vol. **capsules** contg. biol. materials)
IT Brain
(ventral tegmental area, dopamine-secreting cells; manuf. of minimal vol. **capsules** contg. biol. materials)
IT 9002-89-5, **Polyvinyl alcohol** 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-09-2, Poly(vinyl methyl ether) 9003-11-6 9003-39-8, **PVP** 9004-54-0, **Dextran**, biological studies 9005-32-7, Alginic acid 9042-14-2, **Dextran** sulfate 9044-05-7, Carboxymethyl **dextran** 9049-76-7, Hydroxypropyl starch 9050-36-6, Maltodextrin 9057-02-7, Pullulan 9078-46-0, Hydroxypropyl **dextran 25322-68-3** 25702-74-3, Ficoll 55965-52-1, Benzoyldextran
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manuf. of minimal vol. **capsules** contg. biol. materials)

L114 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:649643 HCAPLUS
DN 125:284923
TI **Aerosols** containing **nanoparticle** dispersions
IN **Wood, Ray W.; Decastro, Lan; Bosch, H. William**
PA Nanosystems L.L.C., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9625918	A1	19960829	WO 1996-US2346	19960223 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	CA 2213638	AA	19960829	CA 1996-2213638	19960223 <--
	AU 9649906	A1	19960911	AU 1996-49906	19960223 <--
	EP 810853	A1	19971210	EP 1996-906566	19960223 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 2001502291	T2	20010220	JP 1996-525798	19960223 <--
	US 6264922	B1	20010724	US 1997-948216	19971009 <--
PRAI	US 1995-394103	A	19950224 <--		
	US 1996-589681	A	19960119		
	WO 1996-US2346	W	19960223		

AB An **aerosol** comprising **droplets** of an aq. dispersion of **nanoparticles**, said **nanoparticles** comprising insol. therapeutic or diagnostic agent **particles** having a **surface modifier** on the **surface** is disclosed.
A method for making the **aerosol** and methods for treatment and diagnosis, esp. of edema, using the **aerosol** is also disclosed.
ST **aerosol nanoparticle** dispersion
IT **Pharmaceutical dosage forms**
(**nanocapsules, aerosols** contg. **nanoparticle** dispersions)

IT **Pharmaceutical dosage forms**
(**sprays, aerosols** contg. **nanoparticle** dispersions)
IT 4419-39-0, Beclomethasone **5534-09-8, Beclomethasone dipropionate** 182633-31-4, Win 68209
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**aerosols** contg. **nanoparticle** dispersions)

L114 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:630418 HCAPLUS
DN 125:257236
TI **Aerosols** containing beclomethasone **nanoparticle** dispersions
IN Wiedmann, Timothy S.; **Wood, Ray W.**; **Decastro, Lan**
PA Nanosystems L.L.C., USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-12
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9625919	A1	19960829	WO 1996-US2347	19960223 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 5747001	A	19980505	US 1995-393973	19950224 <--
CA 2213660	AA	19960829	CA 1996-2213660	19960223 <--
AU 9649907	A1	19960911	AU 1996-49907	19960223 <--
EP 810854	A1	19971210	EP 1996-906567	19960223 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11500732	T2	19990119	JP 1996-525799	19960223 <--
PRAI US 1995-393973		19950224 <--		
WO 1996-US2347		19960223		

AB An **aerosol** comprising **droplets** of an aq. dispersion of **nanoparticles**, said **nanoparticles** comprising insol. beclomethasone (I) **particles** having a **surface modifier** on the **surface** thereof. A suspension of 2.5% I.dipropionate in an aq. solns. of **polyvinyl alc.**, as **surface modifier**, was prepd. and used in a **nebulizer**. The **nanoparticles** had a **particle** size distribution of 0.26 .mu.m and the size remained const. throughout the course of the study.
ST pharmaceutical **aerosol** beclomethasone **nanoparticle** dispersion **PVP**; **polyvinyl alc** pharmaceutical **aerosol** beclomethasone **nanoparticle**
IT **Pharmaceutical dosage forms**
(**aerosols, inhalants, aerosols** contg. beclomethasone **nanoparticle** dispersions)
IT 4419-39-0, Beclomethasone **5534-09-8, Beclomethasone dipropionate** 9002-89-5, **Polyvinyl alcohol**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**aerosols** contg. beclomethasone **nanoparticle** dispersions)

L114 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:196877 HCAPLUS

DN 124:242339
TI Liposome-**encapsulated** taxol for tumor treatment
IN Reszka, Regine; Brandl, Martin; Fichtner, Iduna; Warnke, Gernot
PA Max-Delbrueck-Centrum fuer Molekulare Medizin, Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61K031-335
ICS A61K009-127
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 4430593	A1	19960222	DE 1994-4430593	19940820	<--
	DE 4430593	C2	19990114			
	WO 9605821	A1	19960229	WO 1995-DE1163	19950818	<--
	W: JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	EP 776202	A1	19970604	EP 1995-929002	19950818	<--
	EP 776202	B1	20000517			
	R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, NL, SE					
	AT 192924	E	20000615	AT 1995-929002	19950818	<--
	US 6090955	A	20000718	US 1997-793238	19970619	<--
PRAI	DE 1994-4430593	A	19940820	<--		
	WO 1995-DE1163	W	19950818	<--		

OS MARPAT 124:242339
AB Liposomes with a high taxol content, and therefore with high therapeutic effectiveness, and with low neutropenic activity are prepd. by high-pressure homogenization or **aerosolization** of taxol with (a) an amphiphilic lipid, **surfactant**, or emulsifier, (b) a charged lipid, satd. lipid, and/or ether lipid component, (c) a **polymer**, (d) a carrier **liq.**, and (e) optional excipients, e.g. **nanoparticles**. Thus, a lipid film contg. egg phosphatidylcholine 1500 and taxol 30 mg was dispersed in **phosphate**-buffered saline soln. and homogenized at 700 bar for parenteral administration.
ST taxol liposome antitumor
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphiphilic; liposome-**encapsulated** taxol for tumor treatment)
IT Amphiphiles
Brain, neoplasm
Emulsifying agents
Neoplasm inhibitors
Surfactants
(liposome-**encapsulated** taxol for tumor treatment)
IT **Lecithins**
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines
Phosphatidylglycerols
Phosphatidylserines
Phospholipids, biological studies
Polymers, biological studies
Sphingolipids
Sulfatides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-**encapsulated** taxol for tumor treatment)
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ether-linked, amphiphilic; liposome-**encapsulated** taxol for tumor treatment)

IT **Pharmaceutical dosage forms**
(liposomes, liposome-**encapsulated** taxol for tumor treatment)
IT Neoplasm inhibitors
(mammary gland carcinoma, liposome-**encapsulated** taxol for tumor treatment)
IT Neoplasm inhibitors
(melanoma, liposome-**encapsulated** taxol for tumor treatment)
IT Liver, neoplasm
Lung, neoplasm
Neoplasm inhibitors
(metastasis, liposome-**encapsulated** taxol for tumor treatment)
IT Genitourinary tract
(neoplasm, carcinoma, liposome-**encapsulated** taxol for tumor treatment)
IT Mammary gland
(neoplasm, carcinoma, inhibitors, liposome-**encapsulated** taxol for tumor treatment)
IT **Pharmaceutical dosage forms**
(**sprays**, liposome-**encapsulated** taxol for tumor treatment)
IT 33069-62-4, Taxol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-**encapsulated** taxol for tumor treatment)
IT 57-10-3, Palmitic acid, biological studies 57-11-4, **Stearic acid**, biological studies 2197-63-9, Dicetyl **phosphate** 2644-64-6 13699-48-4 **25322-68-3D, PEG**, amphiphilic lipid derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-**encapsulated** taxol for tumor treatment)

L114 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:974924 HCAPLUS
DN 124:37578
TI A **microcalorimetric** investigation of the interaction of **surfactants** with **crystalline** and partially **crystalline** salbutamol sulfate in a model inhalation **aerosol** system
AU Blackett, Peter M.; Buckton, Graham
CS Sch. Pharmacy, Univ. London, London, WC1N 1AX, UK
SO Pharm. Res. (**1995**), 12(11), 1689-93
CODEN: PHREEB; ISSN: 0724-8741
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB The purpose of the work is to study the adsorption of oleic acid and Span 85 (materials frequently used in **aerosols** as **surfactants**) onto partially amorphous and essentially **cryst.** salbutamol sulfate, attempting to understand the behavior of metered dose **inhalers** (MDIs) and observing whether there were any differences in adsorption behavior and if this could be related to the **surface** properties of the powder. Isothermal titrn. **microcalorimetry** was the principal technique used to measure the adsorption behavior of **surfactants** to salbutamol sulfate. A Malvern **particle** size analyzer was also employed to provide size data on the interactions between the **surfactant** and powder suspensions. The calorimetric data revealed that **surfactant** adsorption to the **cryst.** **micronized** powder (78% RH and aged dry sample) produced significant exotherms, whereas adsorption to the partially amorphous **micronized** powder resulted in small heat responses. The differences in adsorption behavior to the partially **cryst.** and **cryst. surfaces** resulted in changes in aggregation behavior. The stability of MDIs varies depending on the **water**

content, **crystallinity** and **surface** compn. of the powder. The advantages of using isothermal titrn. **microcalorimetry** to evaluate this **surface** behavior in such difficult systems was demonstrated.

ST **microcalorimetry surfactant** salbutamol inhalation **aerosol**

IT **Particle size**
Surfactants
(**microcalorimetric** investigation of the interaction of **surfactants** with **cryst.** and partially **cryst** . salbutamol sulfate in inhalation **aerosol** system)

IT 112-80-1, Oleic acid, biological studies 26266-58-0, Span 85 51022-70-9, Salbutamol sulfate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**microcalorimetric** investigation of the interaction of **surfactants** with **cryst.** and partially **cryst** . salbutamol sulfate in inhalation **aerosol** system)

L114 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:843515 HCAPLUS
DN 124:37493
TI **Nebulization** of nanocrystals
AU Wiedmann, T. S.; **DeCastro, L.; Wood, R. W.**
CS University Minnesota, Malvern, PA, USA
SO Proc. Int. Symp. Controlled Release Bioact. Mater. (1995), 22nd, 456-7
CODEN: PCRMEY; ISSN: 1022-0178
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB Nanocrystal technol. provides a suitable means for **nebulizing** aq. dispersions of poorly water **sol.** drugs. **Nebulized** nanocrystals have a dramatically greater fraction of respirable **aerosol particles** in comparison to **nebulized** micronized suspensions. With formulation optimization, nanocrystal dispersions can offer an efficient method of respiratory drug delivery.
ST **nebulization** nanocrystal drug respiratory tract
IT Respiratory tract
(drug delivery to; **nebulization** of nanocrystals)
IT Atomization, spraying
Particle size
(**nebulization** of nanocrystals)
IT Crystallites
(nanocrystals, **nebulization** of nanocrystals)
IT **Pharmaceutical dosage forms**
(**sprays, nebulization** of nanocrystals)

L114 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:528673** HCAPLUS
DN **122:274076**
TI Process for conditioning substances
IN Trofast, Eva Ann-Christin; Briggner, Lars-Erik
PA Astra Aktiebolag, Swed.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-14
ICS A61K009-72; A61K047-12; B01J002-28
CC **63-6** (Pharmaceuticals)
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9505805	A1	19950302	WO 1994-SE780	19940825 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

ZA 9405675	A	19960429	ZA 1994-5675	19940729	<--	
TW 427916	B	20010401	TW 1994-83107152	19940804	<--	
AU 9476264	A1	19950321	AU 1994-76264	19940825	<--	
AU 681186	B2	19970821				
BR 9407320	A	19960416	BR 1994-7320	19940825	<--	
EP 717616	A1	19960626	EP 1994-926421	19940825	<--	
EP 717616	B1	20010321				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE						
CN 1133004	A	19961009	CN 1994-193793	19940825	<--	
CN 1049333	B	20000216				
HU 74000	A2	19961028	HU 1996-447	19940825	<--	
HU 217770	B	20000428				
JP 09501930	T2	19970225	JP 1994-507516	19940825	<--	
JP 2978247	B2	19991115				
PL 176749	B1	19990730	PL 1994-313142	19940825	<--	
RU 2148992	C1	20000520	RU 1996-105935	19940825	<--	
AT 199828	E	20010415	AT 1994-926421	19940825	<--	
ES 2156158	T3	20010616	ES 1994-926421	19940825	<--	
CZ 289018	B6	20011017	CZ 1996-544	19940825	<--	
US 5709884	A	19980120	US 1995-379471	19950130	<--	
NO 9600744	A	19960223	NO 1996-744	19960223	<--	
FI 9600869	A	19960226	FI 1996-869	19960226	<--	
CN 1195523	A	19981014	CN 1997-123049	19971126	<--	
PRAI SE 1993-2777	A	19930827	<--			
WO 1994-SE780	W	19940825	<--			

AB The present invention relates to a process for providing a stable **cryst.** form to a fine-grained substance or a substance mixt., which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation of such a substance or a substance mixt., by a) in case of a substance mixt., prepg. a homogeneous mixt. of the substances; b) **micronizing**, direct pptg. or diminishing by any conventional method the substance or substance mixt. into a **particle** size required for inhalation, the **particle** size being less than 10 .mu.m; c) optionally preparting a homogeneous mixt. of the desired substances when each substance has been introduced from stage b) as sep. fine-grained **particles**; d) conditioning said substance or substance mixt. by treatment with a water contg. vapor phase in a controlled fashion; and e) drying.

ST inhalation pharmaceutical conditioning

IT **Crystal** morphology
Particle size
Size reduction
(process for providing stable **cryst.** form for inhalation pharmaceuticals)

IT Amino acids, biological studies
Carbohydrates and Sugars, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(process for providing stable **cryst.** form for inhalation pharmaceuticals)

IT **Pharmaceutical dosage forms**
(**inhalants**, process for providing stable **cryst.** form for inhalation pharmaceuticals)

IT 50-99-7, D-Glucose, biological studies 56-41-7, Alanine, biological studies 57-48-7, Fructose, biological studies 57-50-1, **Sucrose**, biological studies 59-23-4, Galactose, biological studies 63-42-3 69-65-8, Mannitol 69-79-4, Maltose 87-89-8, Myoinositol 87-99-0,

Xylitol 99-20-7, Trehalose 107-43-7, Betaine 512-69-6, Raffinose 585-88-6, Maltitol 597-12-6, Melezitose 1944-12-3, Fenoterol hydrobromide 4419-39-0, Beclomethasone **5534-09-8**, **Beclomethasone dipropionate** 9005-25-8, Starch, biological studies 13392-18-2, Fenoterol 18559-94-9, Salbutamol 21898-19-1, Clenbuterol hydrochloride 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 23031-32-5, Terbutaline sulfate 30392-40-6, Bitolterol 30392-41-7, Bitolterol mesylate 37148-27-9, Clenbuterol 43229-80-7, Formoterol fumarate 51022-70-9, Salbutamol sulfate 51333-22-3, Budesonide 62929-91-3, Procaterol hydrochloride 72332-33-3, Procaterol 73573-87-2, Formoterol 76596-57-1, Broxaterol 80474-14-2, Fluticasone propionate 81732-46-9, Bambuterol hydrochloride 81732-65-2, Bambuterol 85197-77-9, Tipredane 89365-50-4, Salmeterol 90566-53-3, Fluticasone 94749-08-3, Salmeterol xinafoate 105102-22-5, Mometasone 144459-70-1
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(process for providing stable **cryst**. form for inhalation pharmaceuticals)

L114 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:365085 HCAPLUS
DN 122:170027
TI **Particle** size determination of metered dose **inhalers** with inertial separation methods: Apparatus A and B (BP), Four Stage Impinger and Andersen Mark II Cascade Impactor
AU Holzner, Peter M.; Mueller, Bernd W.
CS Department of Pharmaceutics and Biopharmaceutics, Christian Albrecht University, Kiel, 24118, Germany
SO Int. J. Pharm. (**1995**), 116(1), 11-18
CODEN: IJPHDE; ISSN: 0378-5173
DT Journal
LA English
CC **63-6** (Pharmaceuticals)
AB The **particle** size of pharmaceutical **aerosols** is the main factor governing their deposition in the human respiratory tract. Of the many methods that are available for **particle** size anal. of **aerosols**, inertial methods have been found to give the most representative results, as compared to in vivo conditions. Two devices working on this principle have been included in the British Pharmacopoeia, App. A and App. B. One of their disadvantages is, however, that they only divide the **aerosol particles** into two fractions and do not yield a **particle** size distribution. Therefore, a third device, the Multistage Cascade Impactor no. 1, has addnl. been taken up in the USP. Apart from App. A and B, two devices that comply with this USP monograph were used in this study. The first was a self-made Four Stage Impinger, the second device being the Andersen Mark II Cascade Impactor with eight stages and a preseparator. The aim of this study was to compare the results of **particle** size anal. of different test **aerosol** formulations in metered dose **inhalers** with these four devices. In the first part of the study, one formulation was analyzed with all four methods. There was excellent agreement between App. A and the Four Stage Impinger on the one hand and between App. B and the Andersen Impactor on the other. In the second part of the study, App. A and the Four Stage Impinger were compared in greater detail by sizing five more **aerosol** formulations. There was again excellent agreement in the fine **particle** fractions as detd. with the two methods. By comparing the fraction of **particles** below 2.8 .mu.m addnl., the Four Stage Impinger allowed better distinction between the **aerosol** formulations than App. A. All in all, each of the four devices turned out to be useful for detg. the **particle** size of an **aerosol**. Considering the anal. effort necessary and the amt. of data generated with each of the devices, the Four Stage Impinger

appeared to be the most effective.
ST **particle** size pharmaceutical **inhaler** impinger
IT **Particle size**
(**particle** size detn. of metered dose **inhalers** with inertial sepn. methods)
IT **Pharmaceutical dosage forms**
(**sprays**, metered dose; **particle** size detn. of metered dose **inhalers** with inertial sepn. methods)
IT **5534-09-8**, Beclomethasone 17,21-dipropionate 15826-37-6, Cromolyn sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**particle** size detn. of metered dose **inhalers** with inertial sepn. methods)

L114 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1994:541694** HCAPLUS
DN **121:141694**
TI **Inhaler** system for dispensing drug **particles**
IN Andersson, Jan Anders Roland; Jaegfeldt, Han Aake Ingemar; Trofast, Eva Ann-Christin; Wetterlin, Kjell Ingvar Leopold
PA Aktiebolaget Astra, Swed.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-72
ICS A61K031-135
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9413271	A1	19940623	WO 1993-SE1053	19931207 <--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2148617	AA	19940623	CA 1993-2148617	19931207 <--
	AU 9456634	A1	19940704	AU 1994-56634	19931207 <--
	EP 673244	A1	19950927	EP 1994-902170	19931207 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRAI	SE 1992-3743		19921211 <--		
	WO 1993-SE1053		19931207 <--		

AB The use of a **inhaler** (TURBUHALER or MONOHALER) having the capacity to dispense a high proportion of drug such as .beta.-2-agonists, **corticosteroids** in inhalable powder **particles** up to 10 .mu. is described. Thus, the delivery of budesonide by the **inhaler** at flow of 60 L/min led to greater proportion of fine **particles** than the delivery by a metered-dose **inhaler**.
ST **inhaler** drug **particle**; beta adrenergic agonist **particle inhaler**
IT **Particle size**
(of drug powders, **inhaler** system for delivery in relation to)
IT **Medical goods**
(**inhalers**, drug powders delivery by, in humans)
IT **Pharmaceutical dosage forms**
(powders, **inhalers** for delivery of fine **particles** of, in humans)
IT Adrenergic agonists
(.beta.2-, agonists, **inhalers** for delivery of fine **particles** of, in humans)
IT 18559-94-9, Salbutamol 23031-25-6, Terbutaline 23031-32-5, Terbutaline sulfate 51333-22-3, Budesonide 73573-87-2, Formoterol

RL: BIOL (Biological study)
(**inhalers** for delivery of fine **particles** of, in humans)

L114 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1994:143901** HCAPLUS
DN **120:143901**
TI **Micromeritic** characteristics and agglomeration mechanisms in the **spherical crystallization** of bucillamine by the **spherical** agglomeration and the emulsion solvent diffusion methods
AU Morishima, Kenji; Kawashima, Yoichi; Kawashima, Yoshiaki; Takeuchi, Hirofumi; Niwa, Toshiyuki; Hino, Tomoaki
CS Santen Pharm. Co., Ltd., Osaka, 533, Japan
SO Powder Technol. (**1993**), 76(1), 57-64
CODEN: POTEBX; ISSN: 0032-5910
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB The phys. properties of bucillamine were modified by the application of two **spherical crystn.** techniques -- the **spherical** agglomeration and emulsion solvent diffusion methods. The mechanisms of **spherical** agglomeration and **crystn.** were investigated. In the **spherical** agglomeration method, the **microcryst.** drug ppts. were aggregated via **liq.** bridges of dichloromethane liberated from the **crystn.** solvent system. The growth rates were mainly detd. by the amt. of dichloromethane formulated. In the emulsion solvent diffusion method, the drug was pptd. within finely dispersed **ethanol** drops and these quasi-emulsion **droplets** were transformed into rigid **spherical** agglomerates. The mechanism detg. the structure of the resultant agglomerates was clarified by measuring their mech. strength. The **crystal** binding points within agglomerates produced by the **spherical** agglomeration method were distributed uniformly through the entire cross-section, whereas in the agglomerates prepd. by the emulsion solvent diffusion method, they were localized in the agglomerate **surface** crust.
ST **spherical crystn** bucillamine agglomeration
IT Agglomeration
(bucillamine **spherical crystn.** by, **micromeritic** characteristics and agglomeration mechanisms in)
IT Diffusion
(emulsion solvent, bucillamine **spherical crystn.** by, **micromeritic** characteristics and agglomeration mechanisms in)
IT **Particle size**
(of bucillamine agglomerates)
IT **Crystallization**
(**spherical**, of bucillamine, by agglomeration and emulsion solvent diffusion, **micromeritic** characteristics and agglomeration mechanisms in)
IT 9004-65-3, HPMC
RL: BIOL (Biological study)
(bucillamine **spherical crystn.** by agglomeration in relation to concn. of)
IT 65002-17-7, Bucillamine
RL: BIOL (Biological study)
(**spherical crystn.** of, by agglomeration and emulsion solvent diffusion, **micromeritic** characteristics and agglomeration mechanisms in)

L114 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:546513 HCAPLUS
DN 119:146513

TI Effect of additives on agglomeration in aqueous coating with hydroxypropyl **cellulose**

AU Fukumori, Yoshinobu; Ichikawa, Hideki; Jono, Kaori; Fukuda, Tomoaki; Osako, Yoshifumi
CS Fac. Pharm. Sci., Kobe-Gakuin Univ., Kobe, 651-21, Japan

SO Chem. Pharm. Bull. (**1993**), 41(4), 725-30
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 42

AB **Water-sol**. hydroxypropyl **cellulose** (HPC) was applied to fine lactose powder (53-63 .mu.m) by the Wurster process. The effects of various additives on agglomeration were studied by the binding strength of membrane materials, the **droplet** size and the **surface** morphol. of coated **particles**. The agglomeration was also computer-simulated by a previously reported model. Me **cellulose** (MC) and sodium alginate (ALG) increased the mass median diam. of **droplets** at 10% addn. to HPC, while the other additives exhibited no significant effect on the **droplet** size distribution. The prodn. of coarse **droplets** induced by MC and ALG led to the agglomeration of 76 and 87% cores, resp., though they reduced the binding strength of HPC. **Polyethylene glycol** (**PEG**) reduced the agglomeration by weakening the binding strength of HPC in particular. NaCl, which was incompatible with HPC, reduced agglomeration by hindering HPC from forming homogeneous film. The computer simulation indicated that the smallest sizes of **droplets** causing the agglomeration were 44-71 .mu.m. With MC and ALG the wt. fraction of coarse **droplets** causing the agglomeration reached 5.7 and 4.4%, resp.; however, it was less than 1% with the other additives. Such a minor quantity of **droplets** caused the agglomeration of cores of 18% (**PEG** and NaCl) to 69% (**polyvinyl alc.**). It was suggested that the agglomeration enhancing factor, K, might well reflect the state of fluidization.

ST hydroxypropyl **cellulose** spray coating agglomeration additive

IT Agglomeration
(in spray coating with aq. hydroxypropyl **cellulose**, additives for suppression of, simulation of)

IT **Particle size**
(of **microcapsules** prepd. by spray coating with aq. hydroxypropyl **cellulose**, additives effect on)

IT Granulation
(spray coating with aq. hydroxypropyl **cellulose** in pharmaceutical, agglomeration in, additives for suppression of)

IT **Pharmaceutical dosage forms**
(**microcapsules**, spray coating with aq. hydroxypropyl **cellulose** in prepn. of, agglomeration in, additives for suppression of)

IT Coating process
(spray, of pharmaceuticals, with aq. hydroxypropyl **cellulose**, agglomeration in, additives for suppression of)

IT **Pharmaceutical dosage forms**
(tablets, from hydroxypropyl **cellulose microcapsules**, hardness of, additives in spray coating effect on)

IT 57-50-1, Saccharose, biological studies 57-55-6, **Propylene glycol**, biological studies 121-54-0, Benzethonium chloride 577-11-7, **Aerosol** OT 7647-14-5, Sodium chloride, biological studies 9002-89-5, **Polyvinyl alcohol** 9004-32-4, Sodium CM-**cellulose** 9004-65-3 9004-67-5 9005-38-3, Sodium alginate 9005-65-6, Polysorbate 80 14807-96-6, Talcum, biological studies **25322-68-3**, **Polyethylene glycol**
RL: BIOL (Biological study)

(additive, agglomeration in spray coating with hydroxypropyl **cellulose** suppression by)
IT 51460-26-5, Carbazochrome sodium sulfonate
RL: BIOL (Biological study)
(**microencapsulation** of, by spray coating with hydroxypropyl **cellulose**, agglomeration in, additives for suppression of)
IT 63-42-3, Lactose
RL: BIOL (Biological study)
(spray coating of, with hydroxypropyl **cellulose**, agglomeration in, additives for suppression of)
IT 9004-64-2, Hydroxypropyl **cellulose**
RL: BIOL (Biological study)
(spray coating with, agglomeration in, additives for suppression of)

L114 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1991:639584** HCAPLUS
DN **115:239584**
TI Agglomeration behavior and modification of **spherical crystallization** process of pharmaceuticals by the emulsion-solvent-diffusion method and proposed closed-circuit batch system
AU Kawashima, Yoshiaki; Fude, Cui; Takeuchi, Hirofumi; Niwa, Toshiyuki; Hino, Tomoaki; Kihara, Kazuhiko
CS Dep. Pharm. Eng., Gifu Pharm. Univ., Gifu, 502, Japan
SO Yakugaku Zasshi (**1991**), 111(8), 451-62
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
CC **63-6** (Pharmaceuticals)
AB Agglomeration mechanism of the **spherical crystn.** of a **water sol.** drug by the emulsion solvent diffusion method was investigated with a mixed system of 2 or 3 partially miscible solvents, i.e., bridging **liq.**-poor solvent system or good solvent-bridging **liq.**-poor solvent system. When bridging **liq.** (or plus good solvent) soln. of the drug was poured into poor solvent (=dispersing medium) under agitation, quasi emulsion **droplets** of bridging **liq.** or good solvent were produced. The diffusion of bridging **liq.** or good solvent from the emulsion **droplet** into the dispersing medium induced the **crystn.** of drug, which was clearly monitored by an x-ray diffraction anal. Seeding the drug **crystals** to the system enhanced the solidification of emulsion **droplets**, resulting in improved agglomeration. The agglomerated **crystals** ha the most thermodynamically stable **cryst.** form. Both hydrophilic and hydrophobic **polymers** could be copptd. into the agglomerated **crystals** to modify the physicochem. properties of raw **crystals** of the drug. A closed batch operation system was proposed to use repeatedly the dispersing medium recovered after each operation for industrialization.
ST **spherical crystn** drug method; emulsion solvent diffusion method **crystn**
IT Diffusion
(in emulsion in drug **spherical crystn.** with closed-circuit system)
IT **Particle size**
(of drug **spherical crystal** agglomerates, additive in emulsion solvent diffusion prepn. method effect on)
IT Agglomeration
(of drug **spherical crystals**, additive in emulsion solvent diffusion prepn. method effect on)
IT Solvent effect
(on drug **spherical crystn.** by emulsion diffusion method with closed-circuit system)
IT **Crystallization**

(**spherical**, of pharmaceuticals, by emulsion diffusion method with closed-circuit system)

IT 60-29-7, Ethyl ether, properties 64-17-5, **Ethanol**, properties 67-56-1, Methanol, properties 108-20-3, Isopropyl ether 108-21-4, Isopropyl acetate 110-82-7, Cyclohexane, properties 141-78-6, Ethyl acetate, properties
RL: PRP (Properties)
(systems, for drug **spherical crystn.** by emulsion diffusion method)

L114 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:13577 HCAPLUS
DN 110:13577
TI Pharmaceutical **microcapsules** incorporating a lipid-**soluble surfactant** as a drug release controlling agent
IN Boyes, Robert Nichol; Tice, Thomas Robert; Gilley, Richard Mac; Pledger, Kenneth Lawrence
PA Innovata Biomed Ltd., UK
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K009-50
ICS A61K009-72
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 257915	A1	19880302	EP 1987-307115	19870811	<--
	EP 257915	B1	19930310			
	R: ES, GR					
	WO 8801165	A1	19880225	WO 1987-GB566	19870811	<--
	W: AT, AU, BB, BG, BR, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US					
	RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG					
	AU 8777549	A1	19880308	AU 1987-77549	19870811	<--
	AU 612591	B2	19910718			
	ZA 8705937	A	19880427	ZA 1987-5937	19870811	<--
	EP 318492	A1	19890607	EP 1987-905237	19870811	<--
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
	JP 01503534	T2	19891130	JP 1987-504741	19870811	<--
	JP 2765700	B2	19980618			
	CA 1302258	A1	19920602	CA 1987-544224	19870811	<--
	AT 86482	E	19930315	AT 1987-307115	19870811	<--
	ES 2053549	T3	19940801	ES 1987-307115	19870811	<--
	NO 8801533	A	19880610	NO 1988-1533	19880408	<--
	NO 176784	B	19950220			
	NO 176784	C	19950531			
	DK 8801959	A	19880608	DK 1988-1959	19880411	<--
	DK 171221	B1	19960805			
	GB 2211413	A1	19890705	GB 1989-2288	19890202	<--
	GB 2211413	B2	19900321			
	US 5384133	A	19950124	US 1993-84747	19930629	<--
PRAI	GB 1986-19519		19860811	<--		
	GB 1987-63		19870105	<--		
	EP 1987-307115		19870811	<--		
	WO 1987-GB566		19870811	<--		
	US 1989-317452		19890403	<--		
	US 1992-860584		19920327	<--		

AB Pharmaceutical formulations comprise (1) **microcapsules** which consist essentially of a biocompatible **polymeric** wall material

encapsulating a drug, and (2) a lipid-**sol**. **surfactant** which is mixed with the **microcapsules** or is incorporated within or coats the wall material of the **microcapsules**. Terbutaline sulfate (I) was added to 1.25% by wt. poly(lactide-glycolide) soln. and this mixt. was spray-dried to give **microcapsules**. An **aerosol** contained 100 mg of **microcapsules** loaded with 26.6% by wt. I, 140 mg Span-85, 3.44 g CFCly, 3.44 g C2F2Cl, and 6.88 g CF2Cl2. The airway resistance was measured with a plethysmograph following the administration of the above **aerosol**. The response was depressed but remained const. up to 6 h in comparison to a formulation without **surfactant**; with the latter, the response was delayed by 1 h and declined after 4 h.

ST **sorbitan** trioleate terbutaline controlled release; bronchodilator **microcapsule surfactant** controlled release

IT Peptides, biological studies
RL: BIOL (Biological study)
(bioactive, controlled-release pharmaceutical **microcapsules** contg. lipid-**sol**. **surfactant** and)

IT Antibiotics
Antihistaminics
Antitussives
Bronchodilators
Cardiovascular agents
Cholinergic antagonists
Neoplasm inhibitors
Virucides and Virustats
Corticosteroids, biological studies
Leukotrienes
RL: BIOL (Biological study)
(controlled-release pharmaceutical **microcapsules** contg. lipid-**sol**. **surfactant** and)

IT Anticonvulsants and Antiepileptics
(controlled-release pharmaceutical **microcapsules**-contg. lipid-**sol**. **surfactant** and)

IT **Pharmaceutical dosage forms**
(**aerosols**, controlled-release **microcapsules**-contg.)

IT Bronchodilators
(antiasthmatics, controlled-release pharmaceutical **microcapsules** contg. lipid-**sol**. **surfactant** and)

IT Ion channel blockers
(calcium, controlled-release pharmaceutical **microcapsules** contg. lipid-**sol**. **surfactant** and)

IT **Pharmaceutical dosage forms**
(dry powders, controlled-release **microcapsules**-contg.)

IT **Fatty acids, esters**
RL: BIOL (Biological study)
(**esters**, with **sorbitan**, pharmaceutical **microcapsules** contg. as drug release controlling agent)

IT **Pharmaceutical dosage forms**
(**microcapsules**, controlled-release, contg. **surfactants** as drug-release agents)

IT Adrenergic agonists
(.beta.-, controlled-release pharmaceutical **microcapsules** contg. lipid-**sol**. **surfactant** and)

IT 18559-94-9, Salbutamol 23031-25-6, Terbutaline
RL: BIOL (Biological study)
(controlled-release **microcapsules** contg. lipid-**sol**. **surfactant** and, for inhalation or oral administration)

IT 69-89-6D, Xanthine, derivs. 15826-37-6, Disodium chromoglycate 23031-32-5, Terbutaline sulfate 51022-70-9, Salbutamol sulfate
RL: BIOL (Biological study)

(controlled-release pharmaceutical **microcapsules** contg. lipid-**sol.** **surfactant** and)

IT 12441-09-7D, **Sorbitan, esters** with **fatty acids** 26266-58-0, Span 85
RL: BIOL (Biological study)
(pharmaceutical **microcapsules** contg., as drug release controlling agent)

L114 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1987:20585** HCAPLUS
DN **106:20585**
TI **Microencapsulation**
IN Kawamura, Michio; Okamoto, Hiroshi; Shimada, Taisuke; Sato, Tatsuo; Doi, Yukio; Awano, Mamoru
PA Oji Paper Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM B01J013-02
ICS B41M005-12
ICA C08F220-06
CC 48-3 (Unit Operations and Processes)
Section cross-reference(s): 5, 17, 38, 41, 42, 62, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 61178035	A2	19860809	JP 1985-17715	19850202 <--
JP 04059932	B4	19920924		

AB **Microcapsules** contg. a highly stable emulsion are manufd. by emulsifying hydrophobic core materials into an aq. acidic **terpolymer** (50-200,000 cP at 30.degree.) as an anionic **polymer** electrolyte and then **encapsulating** of the emulsion with polyamines. The **terpolymers** are 55-95:2-20:2-30 (mol%) acrylic acid-acrylonitrile-methacrylamide or -dimethylacrylamide **copolymers**. The polyamine coating materials are formaldehyde-urea **copolymers**. Thus, 100 wt. parts hydrophobic core soln. contg. alkyldiphenylethane 100, **crystal** violet lactone 4, and benzoyl leuco methylene blue 2 parts was emulsified by stirring (9000 rpm) with 100 wt. parts of a hydrophylic **encapsulating** agent contg. 50 wt. parts **water** and 50 wt. parts aq. 21.7% 80:10:10 (wt. ratio) acrylic acid-acrylonitrile-methacrylamide **copolymer**. The formed oil-in-**water** emulsion (av. diam. 4.0 .mu.) was mixed (at 40.degree.) with 100 wt. parts formaldehyde-melamine **prepolymer** (pH 4.5) and then heated 2 h at 60.degree.. The product of 43.4 wt.% **capsule** slurry was stable (180 cp at 30.degree.), had av. emulsified **droplet** diam. 4.0 .mu., and showed good coloring property without much smudging. Those **encapsulating** agents can be applicable for manuf. of emulsions for pharmaceutical, agrochem. bioregulation, cosmetic, food, dye uses as well as for noncarbon sheets.

ST **microencapsulation** agent hydrophyl acrylic **polymer**; polyamine **microcapsule** coating material; electrolyte **polymer** anionic **microencapsulation** agent

IT Electrolytes
(anionic **polymers**, for **microencapsulation**)

IT Hydrophilicity
(of **encapsulating** acidic **terpolymers**, for hydrophobic emulsion)

IT **Capsule, microbial**
(of hydrophobic materials, **encapsulating** acrylic **polymers** for, with polyamine coating materials)

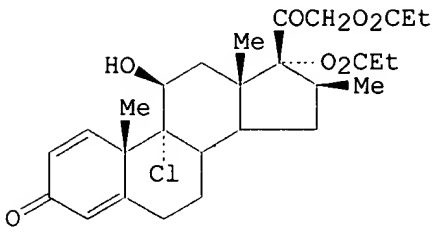
IT **Encapsulation**
(**micro-**, of hydrophobic materials, **encapsulating**

acrylic **polymers** for, with polyamine coating materials)
IT **Pharmaceutical dosage forms**
(**microcapsules**, of hydrophobic materials, **encapsulating** acrylic **polymers** for, with polyamine coating materials)
IT Amines, uses and miscellaneous
RL: USES (Uses)
(poly-, coating materials, for **microcapsules**, **encapsulating terpolymers** for)
IT 31532-31-7 106043-90-7
RL: USES (Uses)
(**encapsulating** agents in emulsions, with polyamine coating materials)
IT 7732-18-5
RL: USES (Uses)
(hydrophilicity, of **encapsulating** acidic **terpolymers**, for hydrophobic emulsion)
IT 9003-08-1, Formaldehyde-melamine **copolymer** 9011-05-6, Formaldehyde-urea **copolymer** 86701-58-8
RL: USES (Uses)
(**microcapsule** coating materials, **encapsulating terpolymer** agents for)
IT 588-59-0D, alkyl derivs. 1249-97-4 1552-42-7, **Crystal** violet lactone
RL: USES (Uses)
(**microcapsule** core materials contg., noncarbon-sheet **encapsulating polymers** in relation to)

L114 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:614099 HCAPLUS
DN 105:214099
TI Physically modified **beclomethasone dipropionate** suitable for use in **aerosols**
IN Jinks, Philip Anthony
PA Riker Laboratories, Inc., USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J005-00
ICS A61K009-72
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 8603750	A1	19860703	WO 1985-GB588	19851216	<--
	W: AU, DK, JP, KR, NO, US					
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
	AU 8653087	A1	19860722	AU 1986-53087	19851216	<--
	AU 587010	B2	19890803			
	EP 205530	A1	19861230	EP 1986-900210	19851216	<--
	EP 205530	B1	19890222			
	R: BE, CH, DE, FR, GB, IT, LI, NL, SE					
	JP 62501706	T2	19870709	JP 1986-500413	19851216	<--
	JP 07014880	B4	19950222			
	JP 07014880	B4	19950222	JP 1985-500413	19851216	<--
	ZA 8509631	A	19870527	ZA 1985-9631	19851217	<--
	ES 550076	A1	19861216	ES 1985-550076	19851218	<--
	CA 1253806	A1	19890509	CA 1985-498011	19851218	<--
	DK 8603917	A	19860818	DK 1986-3917	19860818	<--
	NO 8603321	A	19860818	NO 1986-3321	19860818	<--
	NO 170516	B	19920720			
	NO 170516	C	19921028			

US 4810488 A 19890307 US 1986-902411 19860818 <--
PRAI GB 1984-32063 19841219 <--
WO 1985-GB588 19851216 <--
GI



I

AB A stable **aerosol** formulation of **beclomethasone dipropionate** (I) is prepd. by contacting I with C1-5 alc., reducing the **particle** size of the **cryst.** solvate formed to <10.mu. and dispersing the solvate in chlorofluorocarbon propellants. Suitable propellant mixts. generally comprise combinations of Propellants 11 (CClF3), 12 (CCl2F2) and 114 (C2Cl2F4). Thus, 25 g I was dissolved in 200 mL iso-ProH, and the soln. placed at 0.degree. for 24 h. The resulting solid was filtered and dried, and the product powd. and **micronized** in a Trost fluid energy mill. The solvate (4.441 g) was dispersed in 300 g Propellant 11 contg. 2.221 g **sorbitan** trioleate. This suspension was added to 854 g Propellant 114 and 4839 g Propellant 12 in a scale **aerosol** cold-filling vessel at -60 .degree.. The suspension was filled into 375 Al vials using a fill wt. of 16 g/vial. After 6 mo no significant change had occurred in the quality of the suspensions.

ST **beclomethasone dipropionate** solvate alc **aerosol**

IT **Particle size**
(of **beclomethasone dipropionate** solvates with alcs., **aerosol** formulations in relation to)

IT Alcohols, compounds
RL: PREP (Preparation)
(C1-5, solvates with **beclomethasone dipropionate**, prepn. of, for **aerosol** formulations)

IT **5534-09-8DP**, alc. solvates **105248-33-7P 105248-34-8P 105248-35-9P 105248-36-0P 105248-37-1P 105248-38-2P 105248-39-3P 105248-40-6P**
RL: PREP (Preparation)
(prepn. of, for **aerosol** formulations)

L114 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:529025 HCAPLUS
DN 103:129025
TI Size aspects of metered-dose **inhaler aerosols**
AU Kim, Chong S.; Trujillo, D.; Sackner, M. A.
CS Sch. Med., Univ. Miami, Miami Beach, FL, 33140, USA
SO Am. Rev. Respir. Dis. (**1985**), 132(1), 137-42
CODEN: ARDSBL; ISSN: 0003-0805
DT Journal
LA English
CC **63-8** (Pharmaceuticals)

AB The aerodynamic size distribution of several bronchodilator and **corticosteroid** metered-dose **inhaler** (MDI) **aerosols** was estd. in both dry and humid (90% relative humidity) air environments with a 6-stage cascade impactor. The distribution of

aerosol size that penetrated into a simulated lung model were also measured. The size distributions were approx. log-normal and ranged from 2.4 to 5.5 .mu.m in mass median aerodynamic diam. (MMAD) with geometric std. deviation (GSD) of 1.7 to 2.5 in a dry environment. In humid air, MMAD increased from 1 to 26% above the dry air state, but GSD remained unchanged. The size of **aerosol** delivered by MDI that penetrated into a simulated lung model fell to 2.4 to 2.8 .mu.m in MMAD (GSD, 1.9 to 2.2). MMAD of an **aerosol** of cromolyn Na [15826-37-6] powder dispersed by a Spinhaler increased rapidly with increasing humidity, 5.6 and 10.1 .mu.m in dry and humid air, resp. The factors influencing size of MDI-delivered **aerosols**, including formulation, canister pressure, physicochem. properties of propellants, and design of the valve and actuator orifices are discussed. Effective delivery of MDI-generated **aerosols** into the lung is highly dependent on **particle** dynamics and jet flow, and no single parameter can produce a unique **particle** size and jet pattern.

ST **inhaler aerosol** aerodynamic size distribution; cromolyn powder Spinhaler aerodynamics

IT Humidity
(aeordynamic size distribution of pharmaceutical **aerosols** in relation to)

IT Evaporation
(of **aerosol** propellants, **droplets** size effect on)

IT **Particle size**
(of pharmaceutical **aerosols**, propellants vaporization effect on)

IT Flow
(aerodynamic, of pharmaceutical **aerosols**, humidity effect on)

IT **Pharmaceuticals**
(**aerosols**, aerodynamic size distribution of, humidity effect on)

IT 51-43-4 59-42-7 76-25-5 530-08-5 586-06-1 4419-39-0 7683-59-2 15826-37-6 18559-94-9
RL: BIOL (Biological study)
(metered-dose **inhaler aerosol** contg., aerodynamic size distribution of, humidity effect on)

IT 75-43-4 75-69-4
RL: BIOL (Biological study)
(propellant in metered-dose **inhaler aerosols**, vaporization of, **particle** size effect on)

L114 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN **1982:411823** HCAPLUS
DN **97:11823**
TI Controlled porosity **microcapsules**
IN Lim, Franklin; Moss, Richard D.
PA Damon Corp., USA
SO U.S., 5 pp. Cont. of U.S. Ser. No. 931,177, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC B01J013-02
NCL 252316000
CC **63-5** (Pharmaceuticals)
FAN.CNT 7

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 4322311	A	19820330		US 1980-143932	19800425	<--
	US 4324683	A	19820413		US 1975-606166	19750820	<--
PRAI	US 1975-606166		19750820	<--			
	US 1978-931177		19780804	<--			

AB **Microcapsules** of controlled porosity contg. a biol. active core material were prepd. by emulsifying the core material and a 1st monomer in

aq. soln. in a hydrophobic solvent. A monomer complementary to the 1st and **sol.** in the continuous, hydrophobic phase of the emulsion is added to initiate the interfacial **polymn.** about the aq. **droplets**. The affinity of the 1st monomer is varied by adding a solvent to the continuous phase to vary its polarity. An aq. carrier soln. contg. **poly(vinylpyrrolidone)** [9003-39-8], albumin and 250 .mu.L antisera to thyroxine was mixed with 50 .mu.L tetraethylenepentamine carbonate. The aq. phase was then added to cyclohexane contg. Arlacel as an emulsifier. The 2-phase system was emulsified and a cyclohexane-CHCl3 soln. of terephthaloyl chloride was added to initiate the **polymn.** After 60 s, more of terephthaloyl chloride and CHCl3 were added and the emulsion was centrifuged at the end of 4 min. The **microcapsules**, after discarding the supernatant, were washed with Tween 20. These **capsules** have a pore size large enough to allow free passage of thyroxine which has a mol. wt. of about 777 D but too small to allow leakage of antibody.

ST **microcapsule polymer** porosity

IT Albumins, blood serum
Hemoglobins
RL: BIOL (Biological study)
(carriers for polyamide controlled porosity **microcapsules**)

IT Polyamides, biological studies
RL: PREP (Preparation)
(**microcapsules**, with controlled porosity, prepn. of)

IT **Capsules, pharmaceutical**
(**micro-**, polyamide, with controlled porosity, prepn. of)

IT 9003-39-8 9004-54-0, biological studies **25322-68-3**
25702-74-3
RL: BIOL (Biological study)
(carrier for polyamide controlled porosity **microcapsules**)

IT 24938-70-3P 28213-54-9P 82148-13-8P 82148-76-3P
RL: PREP (Preparation)
(**microcapsules**, with controlled porosity, prepn. of)

L114 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1982:91683 HCAPLUS
DN 96:91683
TI Mixture of an antiinflammatory steroid and a fluorochlorohydrocarbon used as a propulsion agent
IN Tanskanen, Paavo Tapani
PA Orion-Yhtyma Oy, Finland
SO Fr. Demande, 8 pp.
CODEN: FRXXBL
DT Patent
LA French
IC A61K009-12; A61K031-57; A61K047-00
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2482457	A1	19811120	FR 1981-9719	19810515 <--
	FR 2482457	B1	19850104		
	FI 8001610	A	19811120	FI 1980-1610	19800519 <--
	FI 63672	B	19830429		
	FI 63672	C	19830810		
	AT 8101791	A	19851215	AT 1981-1791	19810421 <--
	AT 380791	B	19860710		
	GB 2076422	A	19811202	GB 1981-12683	19810424 <--
	CA 1162852	A1	19840228	CA 1981-376540	19810429 <--
	BE 888822	A1	19811116	BE 1981-204802	19810515 <--
	CH 647408	A	19850131	CH 1981-3165	19810515 <--
	DK 8102184	A	19811120	DK 1981-2184	19810518 <--
	NO 8101686	A	19811120	NO 1981-1686	19810518 <--

NO 155429	B	19861222			
NO 155429	C	19870401			
DE 3119745	A1	19820211	DE 1981-3119745	19810518	<--
ES 502286	A1	19820401	ES 1981-502286	19810518	<--
DD 158856	C	19830209	DD 1981-230036	19810518	<--
CS 221831	P	19830429	CS 1981-3676	19810518	<--
HU 26593	O	19830928	HU 1981-1405	19810518	<--
HU 188093	B	19860328			
PL 127872	B1	19831231	PL 1981-231220	19810518	<--
SU 1184428	A3	19851007	SU 1981-3283353	19810518	<--
SE 8103143	A	19811120	SE 1981-3143	19810519	<--
SE 437766	B	19850318			
SE 437766	C	19850627			
NL 8102457	A	19811216	NL 1981-2457	19810519	<--
JP 57016820	A2	19820128	JP 1981-74331	19810519	<--
US 4347236	A	19820831	US 1981-265333	19810519	<--
PRAI FI 1980-1610		19800519	<--		

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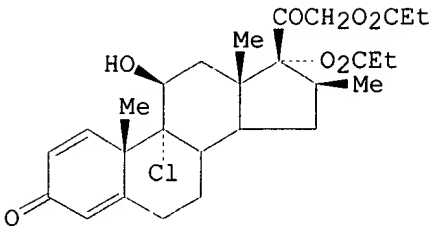

I

AB Antiinflammatory **aerosols** for the respiratory tract contg. finely-divided steroids, e.g. **beclomethasone dipropionate** (I) [**5534-09-8**], were prepd. by an improved process which prevented the growth of the steroid **particles** during storage; this process involved suspending the steroid at 5.degree. to -40.degree. in a small amt. of the blowing agent, e.g. CCl3F [75-69-4] or CCl2F2 [75-71-8], stirring the mixt. for .gtoreq.24 h, and adding the remainder of the blowing agent. Thus, 1.05 g I was suspended in 40 g CCl3F at -25.degree., stirred at -25.degree. for 3 days, then 362.8 g CCl3F was added, the mixt. cooled to 5.degree., stirred with 0.12 g oleic acid for 0.5 h, introduced into a metal container with a regulating valve, and CCl2F2 (10.36 g) introduced under pressure. No significant change was obsd. in the **particle** size of I after 61 days.

ST steroid antiinflammatory **aerosol**; fluorochloromethane steroid **aerosol**; respiratory tract steroid **aerosol**; beclomethasone **aerosol**

IT Respiratory tract
(antiinflammatory steroid **aerosol** formulations for)

IT Steroids, biological studies
RL: BIOL (Biological study)
(inflammation inhibitors, **aerosol** formulations of, blowing agents for)

IT **Particle size**
(of **beclomethasone dipropionate**, prevention of increase of, in **aerosol** cans)

IT Inflammation inhibitors and Antiarthritics
(steroids, **aerosol** formulations of, blowing agents for)

IT **5534-09-8**
RL: PROC (Process)
(**aerosol** formulations of, blowing agents for)

IT 75-69-4 75-71-8

RL: BIOL (Biological study)
(for antiinflammatory steroid **aerosol** formulations)

L114 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1981:36228 HCAPLUS
DN 94:36228
TI Aerodynamic size distribution, hygroscopicity, and deposition estimation of **beclomethasone dipropionate aerosol**
AU Hiller, F. C.; Mazumder, M. K.; Wilson, J. D.; Bone, R. C.
CS Coll. Med., Univ. Arkansas, Little Rock, AR, 72201, USA
SO J. Pharm. Pharmacol. (**1980**), 32(9), 605-9
CODEN: JPPMAB; ISSN: 0022-3573
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB The count median aerodynamic diam. of **beclomethasone dipropionate** [**5534-09-8**] **aerosol** was unchanged on increasing the relative humidity from 24 to 95%, but mass median aerodynamic diam. increased from 2.01 to 2.68 .mu., **particle** no./dose from 41.3 .times. 106 to 78.3 .times. 106, and aerodynamic mass/dose from 23.7 to 60.0 .mu.g. The quantity of active ingredient in the 23.7 .mu.g aerodynamic mass at low humidity was estd. at 19.7 .mu.g. Of a 50 .mu.g dose produced by the metered dose canister, 13% would be expected to deposit in the lower respiratory tract.
ST **beclomethasone dipropionate aerosol**
aerodynamics; humidity beclomethasone **aerosol** aerodynamics
IT **Particle size**
(aerodynamic distribution of, of **beclomethasone dipropionate aerosol**, relative humidity effect on, respiratory tract deposition in relation to)
IT Respiratory tract
(**beclomethasone dipropionate** deposition in, **aerosol** aerodynamic size distribution and relative humidity in relation to)
IT Humidity
(relative, **beclomethasone dipropionate aerosol** aerodynamics response to change in, respiratory tract deposition in relation to)
IT **5534-09-8**
RL: BIOL (Biological study)
(**aerosol** of, aerodynamics of, relative humidity effect on, respiratory tract deposition in relation to)

L114 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2002 ACS
AN 1977:145994 HCAPLUS
DN 86:145994
TI Size analysis of metered suspension pressurized **aerosols** with the Quantimet 720
AU Hallworth, G. W.; Hamilton, R. R.
CS Pharm. Res. Dep., Allen and Hanburys Res. Ltd., Ware, Engl.
SO J. Pharm. Pharmacol. (**1976**), 28(12), 890-7
CODEN: JPPMAB
DT Journal
LA English
CC 64-3 (Pharmaceutical Analysis)
AB A method is described for **particle** sizing of pressurized metered suspension **aerosols** by collection in a settling drum followed by **microscopic** evaluation of the slides with a Quantimet 720 automatic image analyzer. Comparison of different **aerosol** packs of **beclomethasone dipropionate** [**5534-09-8**] (50 .mu.g per dose) and salbutamol [18559-94-9] (100 .mu.g per dose) by this method demonstrated the excellent stability and reproducibility between and within packs. The method gave satisfactory representation of

the distribution of **particles** settling to the drum base although there was more drug deposition of finer size distribution on the drum wall than on the drum base. The Quantimet is suitable for **particle** sizing salbutamol used in prepg. **aerosol** products.

ST **aerosol particle** size analysis; salbutamol
aerosol particle size analysis; beclomethasone
aerosol particle size analysis

IT **Particle size**
(distribution of, of inhalation **aerosols**)

IT **Pharmaceuticals**
(**aerosols, particle** size distribution of, anal. of)

IT **5534-09-8** 18559-94-9
RL: ANST (Analytical study)
(**aerosols** of, **particle** size anal. of)

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FILE 'REGISTRY' ENTERED AT 08:35:13 ON 19 JUL 2002
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DICTIONARY FILE UPDATES:  17 JUL 2002  HIGHEST RN 439210-99-8

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d his l114-

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L114         34 S L108-L113

     FILE 'HCAPLUS' ENTERED AT 08:34:31 ON 19 JUL 2002
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:35:07 ON 19 JUL 2002
L115         11 S E53-E63

     FILE 'REGISTRY' ENTERED AT 08:35:13 ON 19 JUL 2002

=> d ide can tot l115

L115 ANSWER 1 OF 11  REGISTRY  COPYRIGHT 2002 ACS
RN   105248-40-6  REGISTRY
CN   Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-
     oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 2-propen-1-ol (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Propen-1-ol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-
     methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS   STEREOSEARCH
MF   C28 H37 Cl O7 . x C3 H6 O
SR   CA
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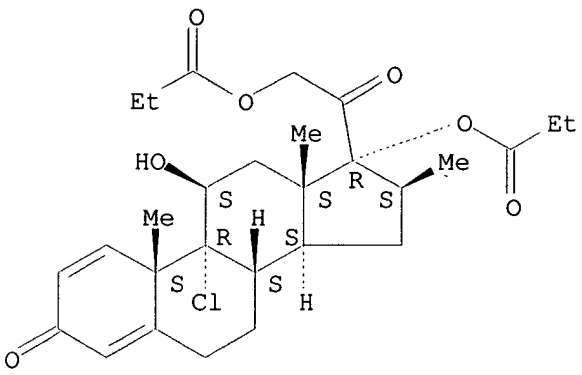
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 107-18-6
CMF C3 H6 O

$H_2C{=}CH{-}CH_2{-}OH$

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

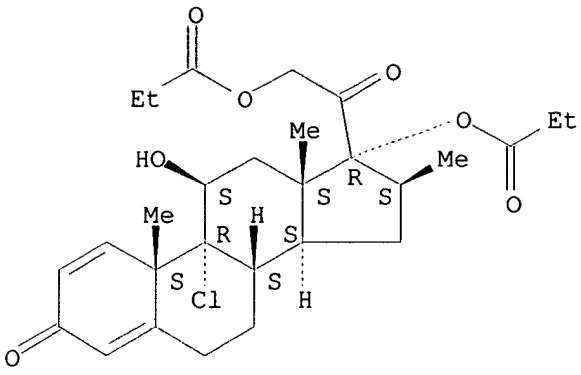
REFERENCE 1: 105:214099

L115 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-39-3** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with methanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C H4 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

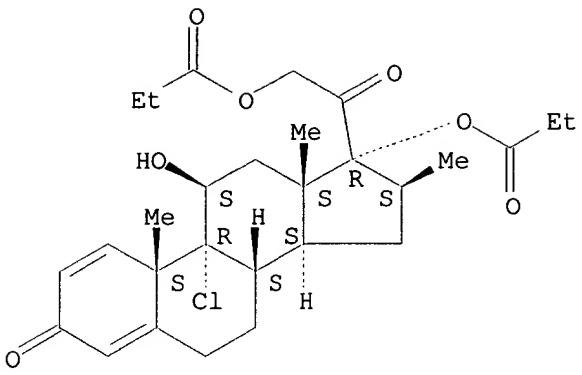
REFERENCE 1: 105:214099

L115 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-38-2** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 1-pentanol (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Pentanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (1:1) (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . C5 H12 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 71-41-0
CMF C5 H12 O

Me— $(CH_2)_4$ —OH

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

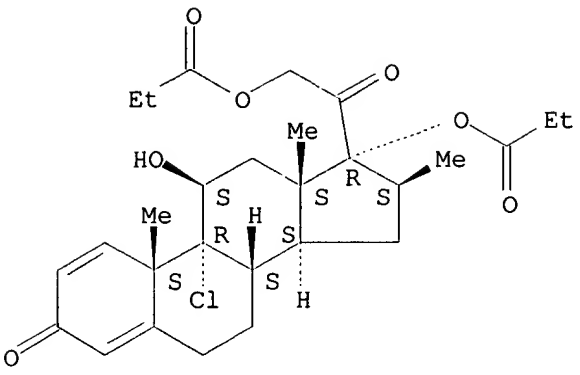
REFERENCE 1: 105:214099

L115 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-37-1** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 2-methyl-1-propanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Propanol, 2-methyl-, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C4 H10 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

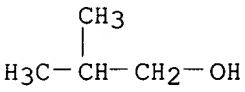
CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 78-83-1
CMF C4 H10 O



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

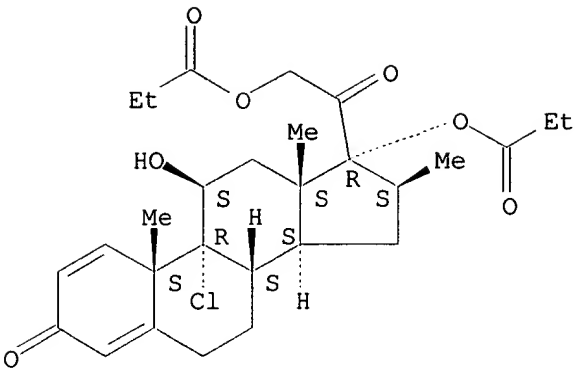
REFERENCE 1: 105:214099

L115 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-36-0** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 1-butanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Butanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C4 H10 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 71-36-3
CMF C4 H10 O

$H_3C-CH_2-CH_2-CH_2-OH$

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

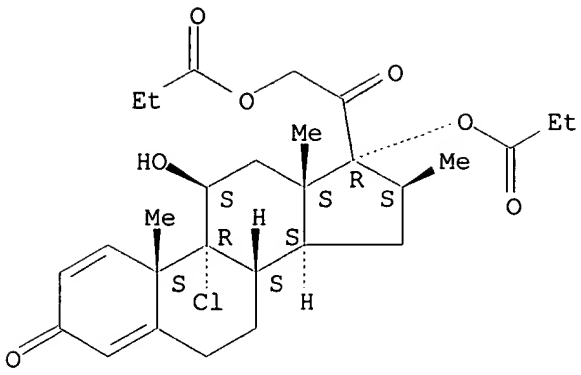
REFERENCE 1: 105:214099

L115 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-35-9** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 1-propanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Propanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C3 H8 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 71-23-8
CMF C3 H8 O

$H_3C-CH_2-CH_2-OH$

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

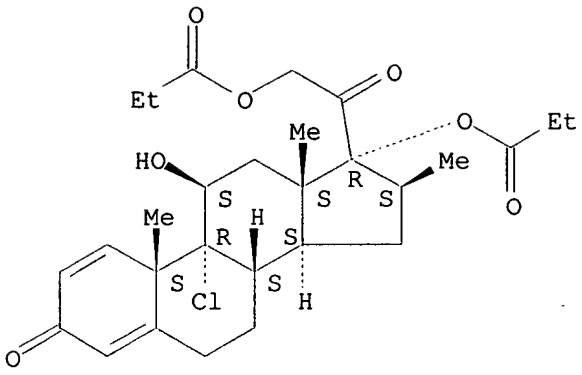
REFERENCE 1: 105:214099

L115 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-34-8** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with ethanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C2 H6 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

H_3C-CH_2-OH

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

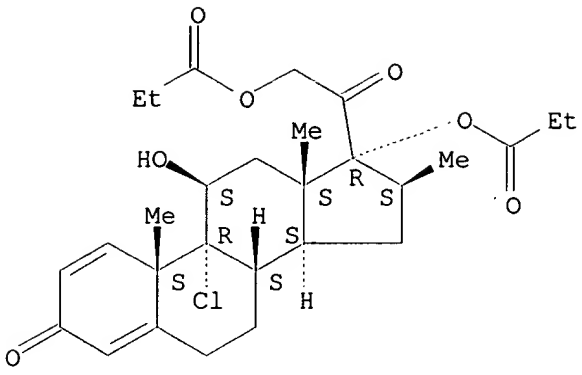
REFERENCE 1: 105:214099

L115 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **105248-33-7** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)-, compd. with 2-propanol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Propanol, compd. with (11.beta.,16.beta.)-9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione (9CI)
FS STEREOSEARCH
MF C28 H37 Cl O7 . x C3 H8 O
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, USPATFULL

CM 1

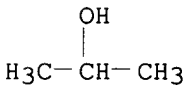
CRN 5534-09-8
CMF C28 H37 Cl O7

Absolute stereochemistry.



CM 2

CRN 67-63-0
CMF C3 H8 O



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 105:214099

L115 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **77011-63-3** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, monohydrate, (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Beclomethasone dipropionate monohydrate
FS STEREOSEARCH
MF C28 H37 Cl O7 . H2 O
LC STN Files: BEILSTEIN*, BIOBUSINESS, CA, CAPLUS, CHEMCATS, CIN, DRUGPAT, PROMT, USPATFULL
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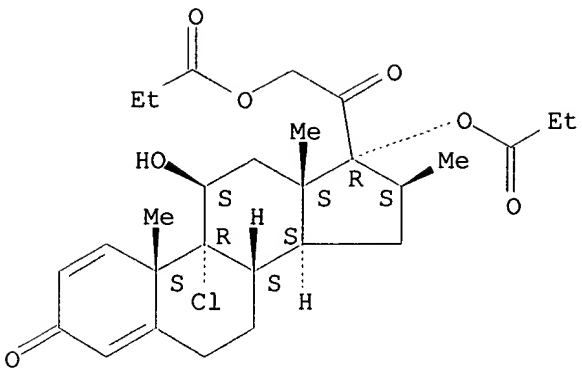
CRN (5534-09-8)

Absolute stereochemistry.



● H_2O

12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:83652

REFERENCE 2: 131:303393

REFERENCE 3: 128:80034

REFERENCE 4: 127:113353

REFERENCE 5: 127:104550

REFERENCE 6: 125:339163

REFERENCE 7: 119:167802

REFERENCE 8: 119:80266

REFERENCE 9: 119:80264

REFERENCE 10: 99:28020

L115 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **25322-68-3** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.,.omega.-Hydroxypoly(ethylene oxide)
CN .alpha.-Hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl)
CN .alpha.-Hydro-.omega.-hydroxypoly(oxyethylene)
CN 1,2-Ethanediol, homopolymer
CN 1660O
CN 1660S
CN Alkox
CN Alkox E 100
CN Alkox E 130
CN Alkox E 160
CN Alkox E 240
CN Alkox E 30
CN Alkox E 45
CN Alkox E 60

CN Alkox E 75
CN Alkox R 1000
CN Alkox R 15
CN Alkox R 150
CN Alkox R 400
CN Alkox SR
CN Antarox E 4000
CN Aquacide III
CN Aquaffin
CN Badimol
CN BDH 301
CN Bradsyn PEG
CN Breox 2000
CN Breox 20M
CN Breox 4000
CN Breox 550
CN Breox PEG 300
CN CAFO 154
CN Carbowax
CN Carbowax 100
CN Carbowax 1000
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CN Carbowax 3350
CN Carbowax 400
CN Carbowax 4000
CN Carbowax 4500
CN Carbowax 4600
CN Carbowax 600
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 9002-90-8
DR 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5, 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0, 101677-86-5, 99264-61-6, 106186-24-7, 112895-21-3, 114323-93-2, 50809-04-6, 50809-59-1, 119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2, 112384-37-9, 70926-57-7, 75285-02-8, 75285-03-9, 77986-38-0, 150872-82-5, 154394-38-4, 79964-26-4, 80341-53-3, 85399-22-0, 85945-29-5, 88747-22-2, 34802-42-1, 107502-63-6, 107529-96-4, 116549-90-7, 156948-19-5, 169046-53-1, 188364-77-4, 188924-03-0, 189154-62-9, 191743-71-2, 201163-43-1, 206357-86-0, 221638-71-7, 225502-44-3, 270910-26-4, 307928-07-0, 356055-70-4, 391229-98-4
MF (C2 H4 O)n H2 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
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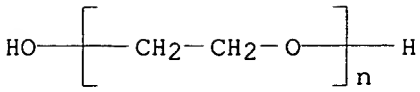
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



61987 REFERENCES IN FILE CA (1967 TO DATE)
16641 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
62063 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:55661

REFERENCE 2: 137:55259

REFERENCE 3: 137:55123

REFERENCE 4: 137:55081

REFERENCE 5: 137:54540

REFERENCE 6: 137:53800

REFERENCE 7: 137:53788

REFERENCE 8: 137:53662

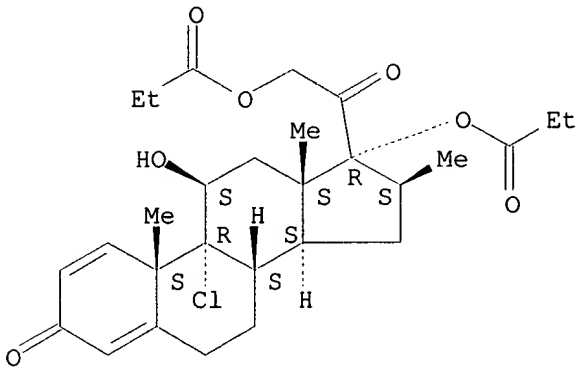
REFERENCE 9: 137:53032

REFERENCE 10: 137:52882

L115 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2002 ACS
RN **5534-09-8** REGISTRY
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pregna-1,4-diene-3,20-dione, 9-chloro-11.beta.,17,21-trihydroxy-16.beta.-methyl-, 17,21-dipropionate (7CI, 8CI)
OTHER NAMES:
CN 9.alpha.-Chloro-16.beta.-methylprednisolone 17,21-dipropionate
CN Aerobec
CN Aldecin AQ nasal
CN Beclate
CN Beclazone
CN Beclazone 250
CN Beclazone 50
CN Beclomet
CN Beclometasone 17,21-dipropionate
CN Beclometasone dipropionate
CN Beclomethasone 17,21-dipropionate
CN Beclomethasone 17.alpha.,21-dipropionate
CN Beclomethasone dipropionate
CN Beclotide
CN Beclotide 100
CN Beclovent
CN Beconase
CN Beconase AQ
CN Becotide
CN Propaderm
CN Propaderm Forte
CN QVAR
CN Sanasthmyl
CN Vancenase
CN Vancenase AQ

CN Vanceril
CN Vanceril DS
FS STEREOSEARCH
DR 34135-07-4
MF C28 H37 Cl O7
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

754 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
757 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:52399

REFERENCE 2: 137:42096

REFERENCE 3: 137:37758

REFERENCE 4: 137:37642

REFERENCE 5: 137:28406

REFERENCE 6: 137:11003

REFERENCE 7: 136:380353

REFERENCE 8: 136:374699

REFERENCE 9: 136:374698

REFERENCE 10: 136:370001

=> fil wpix
FILE 'WPIX' ENTERED AT 09:10:29 ON 19 JUL 2002

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FILE LAST UPDATED: 17 JUL 2002 <20020717/UP>
MOST RECENT DERWENT UPDATE 200245 <200245/DW>
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available in the /ABEX field. An additional search field
/BIX is also provided which comprises both /BI and /ABEX <<<

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http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech tot

L151 ANSWER 1 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 2001-345846 [37] WPIX
CR 1992-417458 [51]; 1995-201854 [27]; 1995-208223 [28]
DNC C2001-107183
TI Chlorofluorocarbon-free **aerosol** formulation, useful for treating asthma, comprises albuterol or **beclomethasone dipropionate** and 1,1,1,2,3,3,3-heptafluoropropane.
DC B05 B07
IN BERRY, J; CHAUDRY, I A; KOPCHA, M; SEQUEIRA, J A
PA (SCHE) SCHERING CORP
CYC 16
PI EP 1092430 A1 20010418 (200137)* EN 14p A61K009-72 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE
ADT EP 1092430 A1 Div ex EP 1992-912490 19920608, Div ex EP 1995-102114 19920608, EP 2000-122297 19920608
FDT EP 1092430 A1 Div ex EP 588897, Div ex EP 656207
PRAI **US 1991-712791 19910610**
IC ICM **A61K009-72**
AB EP 1092430 A UPAB: 20010704
NOVELTY - **Aerosol** formulation comprises:
(a) a medicament selected from albuterol, **beclomethasone dipropionate** and their salts and clathrates;
(b) 1,1,1,2,3,3,3-heptafluoropropane (HFC 227); and optionally
(c) one or more components selected from preservatives, buffers, antioxidants, sweeteners and taste-masking agents.
ACTIVITY - Antiasthmatic.
MECHANISM OF ACTION - None given.
USE - The formulation is useful for treating asthma (claimed).
ADVANTAGE - The formulation is free of chlorofluorocarbons (CFCs) that may damage the ozone layer.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B01-B02; B10-B03A; B10-H02B; B14-K01A
TECH UPTX: 20010704
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Formulation: The medicament is present in an amount of 0.01-1 (especially 0.05-0.5) wt.% and is in the form of a powder with a mean particle size of 1-5 **microm**. The formulation includes an excipient selected from propylene glycol diesters and triglycerides of fatty acids containing 6-12 carbon atoms.

L151 ANSWER 2 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 2000-376273 [32] WPIX
DNC C2000-113708
TI **Aerosol** compositions of aqueous dispersions or powder aggregates of nanoparticulate drugs used for the delivery of e.g. elastase inhibitors, analgesics, anti-fungals or agents used in the treatment of cystic fibrosis, asthma or emphysema.
DC B07
IN **BOSCH, H W**; COOPER, E R; OSTRANDER, K D
PA (NANO-N) NANOSYSTEMS; (ELAN-N) ELAN PHARMA INT LTD
CYC 87
PI WO 2000027363 A1 20000518 (200032)* EN 68p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 2000013469 A 20000529 (200041) A61K009-14 <--
EP 1128814 A1 20010905 (200151) EN A61K009-14 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000027363 A1 **WO 1999-US26799 19991112**; AU 2000013469 A AU 2000-13469 19991112; EP 1128814 A1 **EP 1999-956981 19991112, WO 1999-US26799 19991112**
FDT AU 2000013469 A Based on WO 200027363; EP 1128814 A1 Based on WO 200027363
PRAI **US 1998-190138 19981112**
IC ICM **A61K009-14**
ICS **A61K009-72**
AB WO 200027363 A UPAB: 20000706
NOVELTY - An **aerosol** composition of an aqueous dispersion (I) of nanoparticulate drug (NP) is new.
DETAILED DESCRIPTION - An **aerosol** composition of an aqueous dispersion (I) of nanoparticulate drug NP where each droplet of the **aerosol** comprises at least 1 particle of NP, the droplets are of respirable size and the particles NP comprise a poorly soluble **crystalline** drug (ND) with an average particle size of less than 1000 nm with a surface modifier adsorbed on the surface.
INDEPENDENT CLAIMS are included for:
(1) a spray-dried powder **aerosol** composition (II) comprising aggregates of NP which are of respirable size;
(2) a freeze-dried powder **aerosol** composition (III) comprising aggregates of NP which are of respirable size;
(3) a dry powder nanoparticulate **aerosol** composition (IV) for use in propellant based pressurized metered dose-inhalers (pMDI) comprising aggregates of NP which are of respirable size and a non-aqueous propellant (NAP);
(4) a nanoparticulate **aerosol** composition (V) for use in propellant based pMDI comprising aggregates of NP which are of respirable size and a non-aqueous propellant NAP;
(5) a method of making an aqueous dispersion of nanoparticulate drug particles comprising nebulizing an aqueous dispersion of NP to form an **aerosol**.

(6) a method of making a dry powder nanoparticulate drug composition comprising forming an aqueous dispersion of NP and spray-drying to form a dry powder of aggregates of NP which are of respirable size;

(7) a method of making a dry powder nanoparticulate drug composition comprising milling under non-pressurized conditions a poorly soluble **crystalline** drug and a surface modifier in a non-aqueous medium with a high boiling point to form a composition of NP, and evaporating the non-aqueous medium to form aggregates of NP which are of respirable size;

(8) a method of making a dry powder nanoparticulate drug composition comprising milling under pressurized conditions a poorly soluble **crystalline** drug and a surface modifier in a non-aqueous medium, and evaporating the non-aqueous medium to form aggregates of NP which are of respirable size;

(9) a method of making a nanoparticulate drug composition comprising millling under pressurized conditions a poorly soluble **crystalline** drug and a surface modifier in a non-aqueous medium, and evaporating the non-aqueous medium to form aggregates of NP which are of respirable size;

(10) a method of making a dry powder nanoparticulate drug composition comprising forming an aqueous nanoparticulate dispersion of NP and freeze-drying to form a dry powder of aggregates of NP which are of respirable size.

USE - The composition are used in the delivery into the lungs, particularly into the alveoli, of active agents e.g. proteins, peptides, bronchodilators, corticosteroids, elastase inhibitors, analgesics, anti-fungals, agents used in the treatment of cystic fibrosis, asthma, emphysema, respiratory distress syndrome, chronic bronchitis, chronic obstructive pulmonary disease, organ-transplant rejection, tuberculosis and other infections of the lung, fungal infection, and respiratory illness associated with acquired immune deficiency syndrome (AIDS), oncological drugs, anti-emetics, and cardiovascular drugs.

ADVANTAGE - The compositions allow water-insoluble drugs to be delivered to the deep lung for systemic administration giving rapid absorbtion via the alveoli. The number of drug particles per unit dose is increased providing better drug delivery profiles, and the aqueous **aerosol** dispersions can be nebulized ultrasonically giving smaller particles which penetrate more rapidly than micronized drug compositions.

Dwg.0/10

FS CPI

FA AB

MC CPI: B11-C03; B11-C04; **B12-M01A**; B14-A01; B14-A04; B14-C01; B14-E05; B14-F01; B14-F02; B14-G02C; B14-H01; B14-K01

TECH UPTX: 20000706

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: ND is selected from proteins, peptides, bronchodilators, corticosteroids, elastase inhibitors, analgesics, anti-fungals, agents used in the treatment of cystic fibrosis, asthma, emphysema, respiratory distress syndrome, chronic bronchitis, chronic obstructive pulmonary disease, organ-transplant rejection, tuberculosis and other infections of the lung, fungal infection, and respiratory illness associated with acquired immune deficiency syndrome (AIDS), and oncological drugs, anti-emetics, and cardiovascular drugs. NP have an average particle size of either less than 400 nm, less than 300 nm, less than 250 nm, less than 100 nm or less than 50 nm. (I) comprises a concentration 0.05 - 600 mg/ml ND, preferably 10 mg/ml or more, 100 mg/ml or more, 200 mg/ml or more, 400 mg/ml or more or 600 mg/ml. The droplets of (I) have a MMAD (not defined) of either 2-10 (preferably 2-6) mum , less than 2 mum, or 5-100 (preferably 30-60) mum. (II), (III) comprises a concentration 0.05 - 900 mg/g ND, preferably 10 mg/g or more, 100 mg/g or more, 200 mg/g or more, 400 mg/g or more or 600 mg/g or more or 900 mg/g. The aggregates of NP have a MMAD of either 2-10 (preferably 2-6) mum , less than 2 mum, or 5-100 (preferably 30-60) mum. NAP is a non-chlorofluorocarbon (CFC) propellant.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Manufacture: The

preparation of spray-dried or freeze dried compositions may additionally comprise adding diluent prior to spray-drying or freeze drying the composition.

L151 ANSWER 3 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1996-442833 [44] WPIX
DNC C1996-139331
TI **Aerosols** contg. **nano**-particle dispersions of bioactive agents - use for both therapeutic and diagnostic agents, enables **aerosol** to reach lungs, use in asthma, bronchitis, pneumonia, etc..
DC B07
IN **BOSCH, H W; DE, CASTRO L; WOOD, R W; DECASTRO, L**
PA (NANO-N) NANOSYSTEMS LLC; (ELAN-N) ELAN PHARMA INT LTD
CYC 71
PI WO 9625918 A1 19960829 (199644)* EN 28p A61K009-12 <--
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9649906 A 19960911 (199651) A61K009-12 <--
EP 810853 A1 19971210 (199803) EN A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 2001502291 W 20010220 (200114) 34p A61K009-12 <--
US 6264922 B1 20010724 (200146) A61L009-04 <--
ADT WO 9625918 A1 **WO 1996-US2346 19960223**; AU 9649906 A **AU 1996-49906 19960223**; EP 810853 A1 **EP 1996-906566 19960223, WO 1996-US2346 19960223**; JP 2001502291 W **JP 1996-525798 19960223, WO 1996-US2346 19960223**; US 6264922 B1 **CIP of US 1995-394103 19950224, Cont of US 1996-589681 19960119 , US 1997-948216 19971009**
FDT AU 9649906 A Based on WO 9625918; EP 810853 A1 Based on WO 9625918; JP 2001502291 W Based on WO 9625918
PRAI **US 1996-589681 19960119; US 1995-394103 19950224 ; US 1997-948216 19971009**
REP US 5145684; WO 9208446
IC ICM **A61K009-12**; A61L009-04
ICS A61K009-00; **A61K009-14**; A61K031-216; A61K031-56; A61K049-04; A61P011-00
AB WO 9625918 A UPAB: 19961104
Aerosol comprises droplets of an aq. dispersion of **nanoparticles**, which contain insoluble therapeutic or diagnostic agent with **surface modifier** on the particle **surface.**

USE - Delivery of bioactive agents to the lungs is partic. important in treatment of respiratory related illnesses, including asthma, emphysema, respiratory distress syndrome, chronic bronchitis, cystic fibrosis, and acquired AIDS including AIDS related pneumonia. The diagnostic agents are for visualisation of the lung by x-ray imaging or MRI. A wide variety of therapeutic agents of all types. and diagnostic agents, can be delivered as **nanoparticle aerosols**; examples are **beclomethasone** and its **dipropionate** (BDP), and the polyiodo cpd. WIN 68209 (benzoic acid, 3,5-bis-acetamido-2,4,6-triiodo-4-(ethyl 3-ethoxy-2-butanoate) ester. Delivery of the **aerosol** is by nebulisation, using known nebulising techniques.

ADVANTAGE - The small size of the particles enables the bioactive agent to reach the lungs, without much less deposition in the mouth and throat or loss by exhalation or in the mucus coating, to be lost later by coughing and/or swallowing, than with larger particles.

Dwg.0/0
FS CPI

FA AB; DCN
MC CPI: B01-B03; B10-B02B; B10-D03; B12-K04A; B12-K04C2; B12-K07; **B12-M01A**; **B12-M01B**; B14-G02A; B14-K01

L151 ANSWER 4 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1996-402113 [40] WPIX
DNC C1996-126377
TI New **aerosols** contg. **beclomethazone nano** -particles - having **surface modifier** thereon are used for delivery to the lungs to treat respiratory illnesses.
DC B01
IN **DE CASTRO, L**; WIEDMANN, T S; **WOOD, R W**; **DECASTRO, L**
PA (NANO-N) NANOSYSTEMS LLC
CYC 71
PI WO 9625919 A1 19960829 (199640)* EN 33p A61K009-12 <--
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9649907 A 19960911 (199651) A61K009-12 <--
EP 810854 A1 19971210 (199803) EN A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5747001 A 19980505 (199825) A61K009-12 <--
JP 11500732 W 19990119 (199913) 29p A61K031-57 <--
ADT WO 9625919 A1 **WO 1996-US2347 19960223**; AU 9649907 A **AU 1996-49907 19960223**; EP 810854 A1 **EP 1996-906567 19960223, WO 1996-US2347 19960223**; US 5747001 A **US 1995-393973 19950224**; JP 11500732 W **JP 1996-525799 19960223, WO 1996-US2347 19960223**
FDT AU 9649907 A Based on WO 9625919; EP 810854 A1 Based on WO 9625919; JP 11500732 W Based on WO 9625919
PRAI **US 1995-393973 19950224**
REP US 5145684
IC ICM **A61K009-12**; A61K031-57
ICS **A61K009-72**; A61K047-30
AB WO 9625919 A UPAB: 19990416
An **aerosol** comprising droplets of an aq. dispersion of **nano**-particles comprising insoluble **beclomethazone** particles having a **surface modifier** on their **surface**, is new.
USE - **Beclomethazone** is used in the treatment of respiratory illnesses e.g. seasonal or perennial rhinitis including allergic and non-allergic (vasomotor) rhinitis. Admin. is to the respiratory system, by **aerosol**, such that the medicament reaches the lungs.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B01-B02; B04-C03B; **B12-M01A**; B14-K01

L151 ANSWER 5 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1996-371106 [37] WPIX
DNC C1996-117682
TI Powders for use in dry powder inhalers - comprise active particles, carrier particles, and an additive material (such as leucine) which promotes release of active particles on actuation of the inhaler.
DC B07
IN STANIFORTH, J N
PA (COOR-N) CO-ORDINATED DRUG DEV LTD; (VECT-N) VECTURA LTD
CYC 72
PI WO 9623485 A1 19960808 (199637)* EN 74p A61K009-00

RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN

AU	9645456	A	19960821 (199648)			A61K009-00	
ZA	9600721	A	19961030 (199649)		71p	A61K000-00	
NO	9703502	A	19970930 (199750)			A61K009-72	<--
EP	806938	A1	19971119 (199751)	EN		A61K009-00	
	R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV MC NL PT SE SI						
FI	9703151	A	19970930 (199751)			A61K000-00	
BR	9607490	A	19971223 (199806)			A61K009-00	
CZ	9702443	A3	19980114 (199810)			A61K009-00	
SK	9701036	A3	19980114 (199812)			A61K009-00	
AU	699131	B	19981126 (199908)			A61K009-00	
JP	10513174	W	19981215 (199909)		57p	A61K009-72	<--
NZ	300654	A	19990225 (199914)			A61K009-00	
HU	9802209	A2	19990301 (199916)			A61K009-00	
KR	98701844	A	19980625 (199924)			A61K009-00	
MX	9705847	A1	19980801 (200014)			A61K009-00	
US	6153224	A	20001128 (200063)			A61K009-14	<--
EP	1159955	A1	20011205 (200203)	EN		A61K009-00	
	R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV MC NL PT SE SI						
CN	1179097	A	19980415 (200220)			A61K009-00	

ADT WO 9623485 A1 WO 1996-GB215 19960131; AU 9645456 A AU 1996-45456 19960131; ZA 9600721 A ZA 1996-721 19960131; NO 9703502 A WO 1996-GB215 19960131, NO 1997-3502 19970730; EP 806938 A1 EP 1996-901439 19960131, WO 1996-GB215 19960131; FI 9703151 A WO 1996-GB215 19960131, FI 1997-3151 19970730; BR 9607490 A BR 1996-7490 19960131, WO 1996-GB215 19960131; CZ 9702443 A3 WO 1996-GB215 19960131, CZ 1997-2443 19960131; SK 9701036 A3 WO 1996-GB215 19960131, SK 1997-1036 19960131; AU 699131 B AU 1996-45456 19960131; JP 10513174 W JP 1996-523350 19960131, WO 1996-GB215 19960131; NZ 300654 A NZ 1996-300654 19960131, WO 1996-GB215 19960131; HU 9802209 A2 WO 1996-GB215 19960131, HU 1998-2209 19960131; KR 98701844 A WO 1996-GB215 19960131, KR 1997-705241 19970731; MX 9705847 A1 MX 1997-5847 19970731; US 6153224 A WO 1996-GB215 19960131, US 1997-875391 19970925; EP 1159955 A1 Div ex EP 1996-901439 19960131, EP 2001-120610 19960131; CN 1179097 A CN 1996-192676 19960131

FDT AU 9645456 A Based on WO 9623485; EP 806938 A1 Based on WO 9623485; BR 9607490 A Based on WO 9623485; CZ 9702443 A3 Based on WO 9623485; AU 699131 B Previous Publ. AU 9645456, Based on WO 9623485; JP 10513174 W Based on WO 9623485; NZ 300654 A Based on WO 9623485; HU 9802209 A2 Based on WO 9623485; KR 98701844 A Based on WO 9623485; US 6153224 A Based on WO 9623485; EP 1159955 A1 Div ex EP 806938

PRAI **GB 1995-21937 19951026; GB 1995-1841 19950131**

REP GB 2269992; WO 8705213; WO 9500127; WO 9511666

IC ICM A61K000-00; A61K009-00; **A61K009-14; A61K009-72**
ICS A61F013-02; **A61K009-12; A61K009-50**

AB WO 9623485 A UPAB: 19960918

Powder for use in a dry powder inhaler, comprises **active** particles (APs) and carrier particles (CPs) for carrying the APs. The powder also comprises additive material (AM) on the **surfaces** of the CPs to promote release of the APs from the CPs on actuation of the inhaler. The powder is such that the APs are not liable to be released from the CPs before actuation of the inhaler.

Pref. powder includes not more than 5 wt.% of AM. The CPs are comprised of one or more **crystalline** sugars (esp. lactose). All of the CPs have a dia. of 20-1,000 mu. The AM comprises amino acids (esp. leucine), (poly)peptides with a mol. wt. of 0.25-1,000 kDa, a phospholipid (esp. soya lecithin), a **surfactant**, an anti-adherent material, and/or an anti-friction agent. The AM is in the form of particles, 95 wt.% of which have a dia. less than 100 **microns**. The AM forms a discontinuous covering on the surfaces of the CPs, but saturates the

surfaces of the CPs. The mass median dia. of the APs (esp. a beta2-agonist such as salbutamol or **beclomethasone dipropionate** (BDP)) is not more than 10 mu.

USE - The powders may be used for admin. of pharmaceutical active agents by inhalation.

ADVANTAGE - The inclusion of additive material in the powder increases the respirable fraction of the active material.

Dwg.1/3

FS CPI
FA AB; GI; DCN
MC CPI: B01-B03; B04-B01B; B04-C01; B04-D01; B05-B01P; B10-B02B; B10-B03B; **B12-M01B**; B12-M11G; B14-D01

L151 ANSWER 6 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1996-200700 [20] WPIX
CR 1992-381789 [46]
DNC C1996-063371
TI **Microparticles** carrying therapeutic or diagnostic agent - such as peptide(s) or proteins, are useful in dry powder inhalers.
DC B04 B07 D16
IN JOHNSON, R A; SUTTON, A D; HEATH, D; SENIOR, P J
PA (ANDA-N) ANDARIS LTD; (QUAD-N) QUADRANT HEALTHCARE UK LTD
CYC 66
PI WO 9609814 A1 19960404 (199620)* EN 33p A61K009-16 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AU BB BG BR BY CA CN CZ EE FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TT UA UG UZ VN
AU 9535302 A 19960419 (199630)
ZA 9508239 A 19961129 (199702) 31p A61K000-00
NO 9701438 A 19970326 (199726) A61K009-72 <--
FI 9701332 A 19970401 (199727) A61K000-00
EP 783298 A1 19970716 (199733) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CZ 9700924 A3 19970813 (199739)
BR 9509171 A 19970916 (199744)
HU 77373 T 19980330 (199823)
MX 9702357 A1 19970601 (199825) A61K009-16 <--
JP 10506406 W 19980623 (199835) 33p A61K009-16 <--
KR 97705979 A 19971103 (199844)
NZ 292980 A 19990225 (199914)
AU 701440 B 19990128 (199916)
US 5993805 A 19991130 (200003) A61K038-43
RU 2147226 C1 20000410 (200052) A61K009-19
ADT WO 9609814 A1 WO 1995-GB2279 19950926; AU 9535302 A AU 1995-35302 19950926; ZA 9508239 A ZA 1995-8239 19950929; NO 9701438 A WO 1995-GB2279 19950926, NO 1997-1438 19970326; FI 9701332 A WO 1995-GB2279 19950926, FI 1997-1332 19970401; EP 783298 A1 EP 1995-932122 19950926, WO 1995-GB2279 19950926; CZ 9700924 A3 WO 1995-GB2279 19950926, CZ 1997-924 19950926; BR 9509171 A BR 1995-9171 19950926, WO 1995-GB2279 19950926; HU 77373 T WO 1995-GB2279 19950926, HU 1997-2161 19950926; MX 9702357 A1 MX 1997-2357 19970326; JP 10506406 W WO 1995-GB2279 19950926, JP 1996-511495 19950926; KR 97705979 A WO 1995-GB2279 19950926, KR 1997-702043 19970328; NZ 292980 A NZ 1995-292980 19950926, WO 1995-GB2279 19950926; AU 701440 B AU 1995-35302 19950926; US 5993805 A CIP of WO 1992-GB643 19920410, CIP of US 1993-956875 19930315, US 1995-487420 19950607; RU 2147226 C1 WO 1995-GB2279 19950926, RU 1997-106769 19950926
FDT AU 9535302 A Based on WO 9609814; EP 783298 A1 Based on WO 9609814; CZ 9700924 A3 Based on WO 9609814; BR 9509171 A Based on WO 9609814; HU 77373 T Based on WO 9609814; JP 10506406 W Based on WO 9609814; KR 97705979 A Based on WO 9609814; AU 701440 B Previous Publ. AU 9535302, Based on WO 9609814; US 5993805 A CIP of US 5518709; RU 2147226 C1 Based on WO 9609814
PRAI **EP 1994-307126 19940929; GB 1991-7628 19910410**

REP 1.Jnl.Ref; EP 606486; EP 611567
IC ICM A61K000-00; **A61K009-16**; A61K009-19; **A61K009-72**; A61K038-43
ICS A61K009-00; **A61K009-14**; **A61K009-50**; A61K038-00; A61M015-00; A61P011-00
AB WO 9609814 A UPAB: 20001018
Smooth, spherical, water-soluble **microparticles**, at least 90% of which have a mass median particle size of 1-10 mu m, are for use in therapy or diagnosis. Also claimed is an inhaler device for the delivery of the above therapeutic agent via the pulmonary airways.
USE - The **microparticles** are spray-dried for the delivery of biotechnology prods. such as therapeutics based on rDNA technology.
ADVANTAGE - Admin. of peptides and proteins from the rDNA industry is made possible, avoiding the problems associated with oral and nasal delivery. Spray-drying the particles inhibits denaturation and conversion to polymers. The **microparticles** may be used in dry powder inhalers since they possess echogenicity, pressure resistance, low toxicity and non-immunogenicity.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-B01B; B04-C01; B04-D02; B04-N04; B12-K04A; **B12-M01B**; B12-M10B; B12-M11G; D05-A02; D05-H09

L151 ANSWER 7 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-336790 [43] WPIX
DNC C1995-148478
TI Inhalable drug powder, esp. for treating respiratory disorders - comprising **microfine** drug particles and lactose pellet formed from **microfine** particles, e.g. for treating asthma.
DC B01 B07
IN HALLWORTH, G W
PA (GLAX) GLAXO GROUP LTD
CYC 64
PI WO 9524889 A1 19950921 (199543)* EN 17p A61K009-00 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA US UZ VN
AU 9520689 A 19951003 (199602) A61K009-00 <--
ZA 9502049 A 19960228 (199614) 15p A61K000-00
EP 750492 A1 19970102 (199706) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 750492 B1 20001018 (200053) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU MC NL PT SE SI
DE 69519157 E 20001123 (200101) A61K009-00
US 6183782 B1 20010206 (200109) A61K009-16 <--
ES 2152394 T3 20010201 (200112) A61K009-00
ADT WO 9524889 A1 WO 1995-EP917 19950313; AU 9520689 A AU 1995-20689 19950313; ZA 9502049 A ZA 1995-2049 19950313; EP 750492 A1 EP 1995-913091 19950313, WO 1995-EP917 19950313; EP 750492 B1 EP 1995-913091 19950313, WO 1995-EP917 19950313; DE 69519157 E DE 1995-619157 19950313, EP 1995-913091 19950313, WO 1995-EP917 19950313; US 6183782 B1 WO 1995-EP917 19950313, US 1996-702700 19960913; ES 2152394 T3 EP 1995-913091 19950313
FDT AU 9520689 A Based on WO 9524889; EP 750492 A1 Based on WO 9524889; EP 750492 B1 Based on WO 9524889; DE 69519157 E Based on EP 750492, Based on WO 9524889; US 6183782 B1 Based on WO 9524889; ES 2152394 T3 Based on EP 750492
PRAI **GB 1994-4945 19940315**
REP WO 8705213
IC ICM A61K000-00; A61K009-00; **A61K009-16**
AB WO 9524889 A UPAB: 19951102
A pharmaceutical powder compsn. suitable for inhalation comprises

microfine particles of medicament (I) and at least one lactose pellet of dia. 10-1500 (pref. 150-1000) **microns**, consisting of **microfine** lactose particles. Also claimed is an inhalation device contg. the compsn..

USE - The compsn. is esp. for treating respiratory disorders, using an antiallergic, bronchodilator or antiiflammatory steroid (or mixt.) (esp. salmeterol xinafoate, salbutamol sulphate, flucatisone propionate or **beclomethasone dipropionate**) as (I) (all claimed). The compsn. may be used for treating mild, moderate or severe acute or chronic symptoms or for prophylaxis, e.g. of asthma. Numerous other drugs (I) (e.g. various analgesics, antiinfectives or antiallergics) are mentioned in the disclosure.

ADVANTAGE - All the **microfine** particles of (I) and lactose are potentially available for inhalation (I) is uniformly distributed. The compsn. gives good respirable drug delivery, e.g. in a ''Turbohaler'' (RTM) inhalation device.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-J02; B10-A07; B12-M11G; B14-C03; B14-G02A; B14-K01

L151 ANSWER 8 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-187008 [25] WPIX
CR 1992-417459 [51]; 1995-201853 [27]; 2000-367872 [32]
DNC C1995-086859
TI New non-chloro fluorocarbon **aerosol** formulations - contains mometasone furoate and 1,1,1,2-tetra fluoroethane as a propellant, useful for treating asthma.
DC B01 B07
IN BERRY, J; CHAUDRY, I A; KOPCHA, M; SEQUEIRA, J A
PA (SCHE) SCHERING CORP
CYC 16
PI EP 653205 A1 19950517 (199525)* EN 14p A61K009-72 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE
ADT EP 653205 A1 Related to EP 1992-913922 19920608, EP 1995-101762 19920608
PRAI **US 1991-712789 19910610**
REP 3.Jnl.Ref; EP 372777; WO 9104011
IC ICM **A61K009-72**
ICS A61K031-58
AB EP 653205 A UPAB: 20000706

Aerosol formulation (A), comprises mometasone furoate, 1,1,1,2-tetrafluoroethane and opt. one or more of the following e.g. **surfactants**, buffers, antioxidants, sweeteners and taste-masking agents.

(A) should comprise mometasone furoate in an amt. 0.01-1 (pref. 0.03-0.7 wt.% and esp. 0.05-0.5) wt.%. It is in powder form having a mean particle size of 1-5 **microns**. The pref. formulation should also contain 1,1,1,2-tetrafluoroethane as the propellant, together with a **surfactant** and excipient.

USE/ADVANTAGE - Formulations are used to treat asthma, orally or nasally, and can be used to deliver many classes of cpds. e.g. bronchodilators, antiinflammatory cpds., antihistamines, antiallergics, analgesics, antitussives, antiangina cpds., steroids, corticosteroids, vasoconstrictors, antibiotics. More specific cpds. which can be pref. used are albuterol, mometasone furoate, **beclomethasone dipropionate** isoproterenol, heparin, terbutaline, rimiterol, perbuerol, disodium cromoglycate, isoprenaline, adrenaline, pentamidine and ipratropium bromide.

Formulations are free of CFC's and cause less environmental pollution and therefore less ozone depletion, on their disposal. The propellant has improved the stability and compatibility with the medicament and valve component. The formulation is easily mfd..

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B01-B03; B10-H02B; **B12-M01A**; B14-K01A

L151 ANSWER 9 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-180525 [24] WPIX
CR 1990-180559 [24]; 1992-278075 [34]; 2000-294921 [26]
DNC C1995-083594
TI Medicinal **aerosol** formulation free of chloro-fluorocarbon - comprise medicament, 1,1,1,2-tetra fluoroethane, **surface active** agent and a cpd. having high polarity than the tetra fluoroethane.
DC A96 B05 B07
IN GREENLEAF, D J; PUREWAL, T S
PA (RIKL) RIKER LAB INC
CYC 10
PI EP 653204 A2 19950517 (199524)* EN 10p A61K009-12 <--
R: BE CH DE ES FR GB IT LI NL SE
EP 653204 A3 19951115 (199618) <--
ADT EP 653204 A2 Related to EP 1992-201264 19891127, EP 1995-200166 19891127; EP 653204 A3 EP 1995-200166 19891127
FDT EP 653204 A3 Related to EP 499344
PRAI **GB 1988-28477 19881206**
REP 1.Jnl.Ref; DE 2737132; GB 2046093; US 4174295; WO 9007333
IC ICM **A61K009-12**
ICS **A61K009-72**; A61K047-00; A61M011-04; C09K003-30
AB EP 653204 A UPAB: 20000531
An **aerosol** formulation comprises a medicament, 1,1,1,2-tetrafluoroethane (TFE), a **surface active** agent and at least one cpd. having higher polarity than TFE.
USE - The addn. of the higher polarity increased amts. of **surfactant** may be dissolved compared to their solubility in TFE alone. The **surfactant** allows the prepn. of stable, homogeneous suspensions of drug particles, and may assist in obtaining stable soln. formulations of certain drugs. Admin. is by oral or nasal inhalation, the formulation being a soln. or suspension of medicament particles having median particle size less than 10 **micron**.
ADVANTAGE - In contrast to prior art, the new compsns. do not require the presence of Freon 22, Freon 32 or Freon 143a and are substantially free of chlorofluorocarbons.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-B01C1; B04-C03C; B04-C03D; B10-E04C; B10-H02B; B10-J02; **B12-M01A**

L151 ANSWER 10 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-106650 [14] WPIX
CR 1992-342221 [42]; 1995-384025 [50]; 1999-179930 [15]
DNC C1995-048553
TI Prodn. of stable **crystalline** fine grained substance for drugs admin. by inhalation - by **micronising**, direct pptn. or diminishing substance(s), treating with water contg. vapour phase and drying.
DC B05 B07
IN BRIGGNER, L; TROFAST, E A; TROFAST, E; BRIGGNER, L E; TROFAST, E A C
PA (ASTR) ASTRA AB; (ASTR) ASTRA AG; (ASTR) ASTRAZENECA AB; (ASTR) ASTRA PUBL AB
CYC 62
PI WO 9505805 A1 19950302 (199514)* EN 22p A61K009-14 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK

TJ TT UA US UZ VN

AU	9476264	A	19950321	(199526)		A61K009-14	<--
NO	9600744	A	19960223	(199619)		A61K000-00	
FI	9600869	A	19960226	(199620)		A61K000-00	
BR	9407320	A	19960416	(199622)		A61K009-14	<--
CZ	9600544	A3	19960515	(199627)		A61K009-14	<--
EP	717616	A1	19960626	(199630)	EN	A61K009-14	<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						
ZA	9405675	A	19960626	(199631)	21p	A61K000-00	
HU	74000	T	19961028	(199702)		A61K009-14	<--
SK	9600234	A3	19970205	(199715)		A61K009-14	<--
JP	09501930	W	19970225	(199718)	17p	A61K009-14	<--
US	5637620	A	19970610	(199729)	6p	A61K031-16	
NZ	273090	A	19970624	(199732)		A61K009-14	<--
AU	681186	B	19970821	(199742)		A61K009-14	<--
CN	1133004	A	19961009	(199802)		A61K009-14	<--
US	5709884	A	19980120	(199810)	7p	A61K009-14	<--
SG	47760	A1	19980417	(199827)		A61K009-14	<--
CN	1195523	A	19981014	(199909)		A61K031-19	
JP	2978247	B2	19991115	(199954)	6p	A61K009-14	<--
HU	217770	B	20000428	(200030)		A61K009-14	<--
RU	2148992	C1	20000520	(200056)		A61K009-14	<--
EP	717616	B1	20010321	(200117)	EN	A61K009-14	<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU MC NL PT SE						
DE	69426934	E	20010426	(200130)		A61K009-14	<--
ES	2156158	T3	20010616	(200141)		A61K009-14	<--
TW	427916	A	20010401	(200156)#		A61K009-16	<--
CZ	289018	B6	20011017	(200172)		A61K009-14	<--
MX	201915	B	20010517	(200227)		A61K009-00	
NO	312433	B1	20020513	(200239)		A61K009-14	<--

ADT WO 9505805 A1 WO 1994-SE780 19940825; AU 9476264 A AU 1994-76264 19940825; NO 9600744 A WO 1994-SE780 19940825, NO 1996-744 19960223; FI 9600869 A WO 1994-SE780 19940825, FI 1996-869 19960226; BR 9407320 A BR 1994-7320 19940825, WO 1994-SE780 19940825; CZ 9600544 A3 CZ 1996-544 19940825; EP 717616 A1 EP 1994-926421 19940825, WO 1994-SE780 19940825; ZA 9405675 A ZA 1994-5675 19940729; HU 74000 T WO 1994-SE780 19940825, HU 1996-447 19940825; SK 9600234 A3 WO 1994-SE780 19940825, SK 1996-234 19940825; JP 09501930 W WO 1994-SE780 19940825, JP 1995-507516 19940825; US 5637620 A Div ex US 1995-379471 19950130, US 1995-459660 19950602; NZ 273090 A NZ 1994-273090 19940825, WO 1994-SE780 19940825; AU 681186 B AU 1994-76264 19940825; CN 1133004 A CN 1994-193793 19940825; US 5709884 A WO 1994-SE780 19940825, US 1995-379471 19950130; SG 47760 A1 SG 1996-4257 19940825; CN 1195523 A CN 1997-123049 19971126; JP 2978247 B2 WO 1994-SE780 19940825, JP 1995-507516 19940825; HU 217770 B WO 1994-SE780 19940825, HU 1996-447 19940825; RU 2148992 C1 WO 1994-SE780 19940825, RU 1996-105935 19940825; EP 717616 B1 EP 1994-926421 19940825, WO 1994-SE780 19940825; DE 69426934 E DE 1994-626934 19940825, EP 1994-926421 19940825, WO 1994-SE780 19940825; ES 2156158 T3 EP 1994-926421 19940825; TW 427916 A TW 1994-107152 19940804; CZ 289018 B6 WO 1994-SE780 19940825, CZ 1996-544 19940825; MX 201915 B MX 1994-6483 19940825; NO 312433 B1 WO 1994-SE780 19940825, NO 1996-744 19960223

FDT AU 9476264 A Based on WO 9505805; BR 9407320 A Based on WO 9505805; EP 717616 A1 Based on WO 9505805; HU 74000 T Based on WO 9505805; JP 09501930 W Based on WO 9505805; NZ 273090 A Based on WO 9505805; AU 681186 B Previous Publ. AU 9476264, Based on WO 9505805; US 5709884 A Based on WO 9505805; JP 2978247 B2 Previous Publ. JP 09501930, Based on WO 9505805; HU 217770 B Previous Publ. HU 74000, Based on WO 9505805; RU 2148992 C1 Based on WO 9505805; EP 717616 B1 Based on WO 9505805; DE 69426934 E Based on EP 717616, Based on WO 9505805; ES 2156158 T3 Based on EP 717616; CZ 289018 B6 Previous Publ. CZ 9600544, Based on WO 9505805; NO 312433 B1 Previous Publ. NO 9600744

PRAI **SE 1993-2777 19930827; TW 1994-107152 19940804**

REP EP 508969; WO 8400294; WO 9116882

IC ICM A61K000-00; A61K009-00; **A61K009-14; A61K009-16;** A61K031-16; A61K031-19
ICS **A61K009-12; A61K009-50; A61K009-72;** A61K031-135; A61K031-195; A61K047-12; A61K047-26; B01J002-28; B01J002-30

AB WO 9505805 A UPAB: 20020621
Prodn. of a stable **crystalline** fine grained substance or substance mixt., which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation of the substance or mixt. comprises: (a) for a mixt., preparing a homogeneous mixt. of the substances; (b) **micronising**, direct pptn. or diminishing (by any conventional method) into particle size of < 10 um required for inhalation; (c) opt. preparing a homogeneous mixt. when each substance has been introduced from stage (b) as separate fine-grained particles; (d) conditioning by treatment with a water contg. vapour phase in a controlled fashion; and (e) drying.

For a mixt., the conditioning is pref. a one or multistep process using different relative humidity and temp. combinations. Step (d) is carried out at 0-100 (10-50) deg. C and at a relative humidity so that the phase transition occurs mainly above 35% RH, esp. above 75% RH. The substance or substance mixt. is a drug formulation of a single drug substance or a combination of a drug substance and additive. The substance is e.g.formoterol (FM), salmetenol, salbutanol (SB) bambuterol, terbutaline (TB), fenoterol or clenbuterol.

USE - The prods. have improved physicochemical properties in the dry stage over prior art prods., facilitating the technical handling and increasing the medical value of the formulation used.

ADVANTAGE - The prods. can contain a variety of drugs. Several drugs for treating asthma or other respiratory disorders are ideally applied by inhalation.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: B07-A02B; B10-B03B; B12-M11D

ABEQ US 5637620 A UPAB: 19970716
Formoterol fumarate dihydrate having a particle size less than 10 **microns**, which when subjected to water-containing vapor gives off heat of less than 0.5 J/g.

Dwg.0/1

ABEQ US 5709884 A UPAB: 19980309
Prodn. of a stable **crystalline** fine grained substance or substance mixt., which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation of the substance or mixt. comprises: (a) for a mixt., preparing a homogeneous mixt. of the substances; (b) **micronising**, direct pptn. or diminishing (by any conventional method) into particle size of < 10 um required for inhalation; (c) opt. preparing a homogeneous mixt. when each substance has been introduced from stage (b) as separate fine-grained particles; (d) conditioning by treatment with a water contg. vapour phase in a controlled fashion; and (e) drying.

For a mixt., the conditioning is pref. a one or multistep process using different relative humidity and temp. combinations. Step (d) is carried out at 0-100 (10-50) deg. C and at a relative humidity so that the phase transition occurs mainly above 35% RH, esp. above 75% RH. The substance or substance mixt. is a drug formulation of a single drug substance or a combination of a drug substance and additive. The substance is e.g.formoterol (FM), salmetenol, salbutanol (SB) bambuterol, terbutaline (TB), fenoterol or clenbuterol.

USE - The prods. have improved physicochemical properties in the dry stage over prior art prods., facilitating the technical handling and increasing the medical value of the formulation used.

ADVANTAGE - The prods. can contain a variety of drugs. Several drugs for treating asthma or other respiratory disorders are ideally applied by

inhalation.
Dwg.0/1

L151 ANSWER 11 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-082823 [12] WPIX
DNC C1995-037268
TI Ubidecarenone **microparticle** and **nanoparticle** formulation - provides improved bio-availability and drug carrier system for incorporated active agents, esp. for intravenous admin..
DC A96 B05 B07 C03 C07 D13 D21 P73
IN SIEKMANN, B; WESTESEN, K
PA (WEST-I) WESTESEN K; (SIEK-I) SIEKMANN B; (KNOL) KNOLL AG
CYC 57
PI DE 4327063 A1 19950216 (199512)* 20p C07C050-28 <--
WO 9505164 A1 19950223 (199513) EN 48p A61K009-14 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
AU 9473926 A 19950314 (199525) A61K009-14 <--
EP 711151 A1 19960515 (199624) EN A61K009-14 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
JP 09502963 W 19970325 (199722) 73p A61K009-00
EP 711151 B1 20000503 (200026) EN A61K009-14 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
DE 69424288 E 20000608 (200034) A61K009-14 <--
ES 2145146 T3 20000701 (200036) A61K009-14 <--
US 6197349 B1 20010306 (200115) A61K009-50 <--
ADT DE 4327063 A1 DE 1993-4327063 19930812; WO 9505164 A1 WO 1994-SE728 19940809; AU 9473926 A AU 1994-73926 19940809; EP 711151 A1 EP 1994-923855 19940809, WO 1994-SE728 19940809; JP 09502963 W WO 1994-SE728 19940809, JP 1995-506899 19940809; EP 711151 B1 EP 1994-923855 19940809, WO 1994-SE728 19940809; DE 69424288 E DE 1994-624288 19940809, EP 1994-923855 19940809, WO 1994-SE728 19940809; ES 2145146 T3 EP 1994-923855 19940809; US 6197349 B1 Cont of WO 1994-SE728 19940809, Cont of US 1996-591582 19960207, US 1997-968899 19971106
FDT AU 9473926 A Based on WO 9505164; EP 711151 A1 Based on WO 9505164; JP 09502963 W Based on WO 9505164; EP 711151 B1 Based on WO 9505164; DE 69424288 E Based on EP 711151, Based on WO 9505164; ES 2145146 T3 Based on EP 711151
PRAI **DE 1993-4327063 19930812**
REP 5.Jnl.Ref; DE 3524788; JP 61068412
IC ICM A61K009-00; **A61K009-14**; **A61K009-50**; C07C050-28
ICS A01N025-12; A01N033-18; A01N043-30; A01N053-08; A01N057-14; A01N057-26; **A61K009-12**; **A61K009-51**; A61K031-12; A61K031-19; A61K031-215; A61K031-23; A61K031-56; A61K031-59; A61K047-30; B01F003-00; B01F017-00; B01J013-02; B32B005-16; C07C046-10; C07C050-06
AB DE 4327063 A UPAB: 20010418
Ubidecarenone (coenzyme Q10) particles which have a diameter of 10 nm to 10 mu and which are amorphous at room temp. (20 deg. C) are claimed.

Particles are suitably stabilised using one or more opt. hydrogenated phospholipids, (glyco)sphingolipids, cholanic acid salts, sterols, satd. or unsatd. fatty acids and fatty alcohols as well as their resp. salts, ethoxylated derivs. and ethers and esters (including those derived from sugars), opt. ethoxylated sorbitan esters and ethers, partial fatty acid glycerides, synthetic biocompatible polymers (e.g. block polymers of polyethylene- and polypropylene oxides), amino acids, polypeptides, proteins and peptisators.

USE - Particles are used for the parenteral, oral, peroral, rectal, nasal, pulmonal, ocular and topical admin. of ubidecarenone or other **active** agents in pharmaceutical, dietetic, food, cosmetic and veterinary formulations. The particles may also act as a drug carrier

system for **active** agents which are dissolved, dispersed or solubilised in the particles or adsorbed on their **surface**. They are esp. suitable for i.v. admin. of agents which are difficultly soluble in water, highly lipophilic and/or have low bioavailability. Such agents include antibiotics, e.g. fosfomycin, antihypertonics, e.g. minoxidil, antiphotonics, e.g. dihydro-ergotamine, antimycotics, e.g. ketoconazole, antiinflammatories, e.g. indomethacin, antivirals, e.g. acyclovir, ACE inhibitors, e.g. captopril, beta-blockers, e.g. propanolol, bronchodilators, e.g. ipratropium bromide, Ca antagonists, e.g. diltiazem, cardiac glycosides, e.g. digitoxin, cephalosporins, e.g. ceftizoxime, cytostatics, e.g. cyclophosphamide, hypnotics and sedatives, e.g. flurazepam, psycho-pharmaceuticals, e.g. oxazepam, steroid hormones, e.g. cortisone, vasodilators, e.g. molsidomine, cerebral vasodilators, e.g. di:hydro-ergotoxin, and fat-soluble vitamins.

ADVANTAGE - Compared with prior art formulations, the particles provide improved ubidecarenone dosage forms, esp. for i.v. admin., which increase its bio-availability and enable its controlled distribution in the body. When used as a drug carrier system, the particles avoid disadvantages of conventional systems such as liposomes and fatty emulsions, e.g. embolism formation following i.v. admin. Further, the particles are also simple, safe and economical to produce.

Dwg.0/10

FS CPI GMPI
FA AB; DCN
MC CPI: A12-V01; B04-L02; B12-M11E; B04-L02; C04-L02; B12-M11E; C12-M11E; C04-L02; C12-M11E; D03-H01T; D08-B; D08-B10

L151 ANSWER 12 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1995-044940 [07] WPIX
DNC C1995-020228
TI Inhalable powder or **aerosol** drug formulation - contg. fine drug particles encapsulated in natural amphoteric **surfactant**, pref. phospholipid, to reduce lung irritation.
DC B07 C07
IN PETRI, W; REUL, B
PA (FARH) HOECHST AG
CYC 20
PI EP 634166 A1 19950118 (199507)* DE 4p A61K009-00 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 4323636 A1 19950119 (199508) A61K009-14 <--
CA 2128034 A 19950116 (199516) A61K009-12 <--
JP 07053353 A 19950228 (199517) 4p A61K009-107 <--
US 5663198 A 19970902 (199741) 4p A61K031-34
ADT EP 634166 A1 EP 1994-110734 19940711; DE 4323636 A1 DE 1993-4323636 19930715; CA 2128034 A CA 1994-2128034 19940714; JP 07053353 A JP 1994-161640 19940714; US 5663198 A US 1994-274343 19940713
PRAI **DE 1993-4323636 19930715**
REP EP 465841; US 5230884; WO 9011754; WO 9208446
IC **A61K009-14**; **A61K009-50**; A61K047-24
ICM A61K009-00; A61K009-107; **A61K009-12**; **A61K009-14**; A61K031-34
ICS **A61K009-50**; **A61K009-72**; A61K031-44; A61K047-24
AB EP 634166 A UPAB: 19950223
A drug formulation contains **micronised** particles of a sparingly water-soluble drug (I), encapsulated in a natural amphoteric **surfactant** (II) which forms a micelle-colloidal soln. in water. Also claimed is a preformed **aerosol**, consisting of the above formulation and a chlorine-free, partially fluorinated, pressure-liquefied propellant gas (III) selected from heptafluoropropane (R227), tetrafluoroethane (R134a) and their mixts.

USE - The formulations are useful in inhalable powders or **aerosols** for admin. of (I) having water solubility < 0.01%, such as diuretics (claimed) (e.g. furosemide (claimed), azosemide, piretanide,

bumetanide or torasemide), antimycotics (claimed) e.g. clotrimazole, miconazole, ketoconazole, itraconazole, bifonazole or rilopirox (claimed), antidiabetics (claimed) e.g. glibenclamide, glimepiride or insulin) or antiallergics (e.g. ASS/furosemide combination).

ADVANTAGE - Encapsulation in (II) improves the local compatibility of (I) with pulmonary mucous membranes (by improving wettability), and thus reduces irritation. (II) include **surfactants** almost identical with those natural occurring in pulmonary mucous membranes. The encapsulated particles are not subject to adhesion and agglomeration. They require no flow improving or suspension stabilising additives, thus minimising the amt. of material supplied to the lungs. The formulations are storage-stable. They can be accurately dosed, and are suitable for use with (III), as ozone-friendly propellants.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-B01B; C04-B01B; B10-H02B; C10-H02B; **B12-M01A**; **C12-M01A**; **B12-M01B**; **C12-M01B**; B12-M09; C12-M09; B12-M11; C12-M11; B14-K01; C14-K01
ABEQ US 5663198 A UPAB: 19971013

A drug formulation comprising a chlorine-free, partially fluorinated hydrocarbon formulated with **micronised** particles of a very sparingly water-soluble drug that are sufficiently coated with a natural, physiologically acceptable ampholytic phospholipid **surfactant** that is soluble in water to give a micellar/colloidal solution.

Dwg.0/0

L151 ANSWER 13 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1994-050719 [07] WPIX
DNC C1994-022830
TI Powder compsns. for inhalation, giving reduced side effects - contains a **microfine** drug and a carrier contg. an antistatic agent.
DC A96 B05
IN LEIGHTON, A; SIMPKIN, G T; TRUNLEY, R
PA (RHON) RHONE POULENC RORER LTD; (RHON) RHONE-POULENC RORER LTD
CYC 48
PI GB 2269992 A 19940302 (199407)* 21p A61K009-00 <--
WO 9404133 A1 19940303 (199410) EN 21p A61K009-00 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN
AU 9347256 A 19940315 (199428) A61K009-00 <--
ZA 9305943 A 19940831 (199435) 21p A61K000-00 <--
EP 654991 A1 19950531 (199526) EN A61K009-00 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
NZ 254945 A 19960625 (199631) A61K009-14 <--
JP 08500109 W 19960109 (199642) 24p A61K009-14 <--
EP 654991 B1 19970611 (199728) EN 13p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 678379 B 19970529 (199730) A61K009-00
DE 69311556 E 19970717 (199734) A61K009-00
ES 2106362 T3 19971101 (199750) A61K009-00
IL 106665 A 19980222 (199814) A61K009-72 <--
US 5908639 A 19990601 (199929) A61K009-14 <--
MX 188568 B 19980408 (200027) A61K009-000
ADT GB 2269992 A GB 1992-17312 19920814; WO 9404133 A1 WO 1993-GB1720 19930813; AU 9347256 A AU 1993-47256 19930813; ZA 9305943 A ZA 1993-5943 19930813; EP 654991 A1 EP 1993-918018 19930813, WO 1993-GB1720 19930813; NZ 254945 A NZ 1993-254945 19930813, WO 1993-GB1720 19930813; JP 08500109 W WO 1993-GB1720 19930813, JP 1994-506017 19930813; EP 654991 B1 EP 1993-918018 19930813, WO 1993-GB1720 19930813; AU 678379 B AU 1993-47256 19930813; DE 69311556 E DE 1993-611556 19930813, EP 1993-918018 19930813, WO 1993-GB1720 19930813; ES 2106362 T3 EP 1993-918018 19930813; IL 106665

A IL 1993-106665 19930812; US 5908639 A Cont of WO 1993-GB1720 19930813, Cont of US 1995-381930 19950424, US 1997-821702 19970319; MX 188568 B MX 1993-4975 19930816

FDT AU 9347256 A Based on WO 9404133; EP 654991 A1 Based on WO 9404133; NZ 254945 A Based on WO 9404133; JP 08500109 W Based on WO 9404133; EP 654991 B1 Based on WO 9404133; AU 678379 B Previous Publ. AU 9347256, Based on WO 9404133; DE 69311556 E Based on EP 654991, Based on WO 9404133; ES 2106362 T3 Based on EP 654991

PRAI **GB 1992-17312 19920814**

REP EP 497564; WO 9116038

IC **A61K009-14; A61K009-72**

ICM A61K000-00; A61K009-00; A61K009-000; **A61K009-14; A61K009-72**

ICS A61K031-23; A61K045-08; A61K047-06; A61K047-14; A61K047-20

AB GB 2269992 A UPAB: 19940329

The powder compsn., comprises: (a) a carrier (at least a portion of which is an antistatic agent); and (b) a **microfine** drug.

Pref., the drug is e.g. salbutamol sulphate, triamcinolone acetamide, a calcitonin, budesonide, or a benzamide deriv. of formula (I) (or their salts or N-oxides) where R1 is 1-4C alkyl; R2 is 2-15C alkyl, or a 3-10C mono-, bi- or tricyclic cycloalkyl gp., R3 is e.g. phenyl, naphthyl or heterocyclyl, all opt. substd., Z is O or S.

The component is a sorbitan fatty acid ester, a polyoxyethylene sorbitan fatty acid ester, dioctyl sodium sulphosuccinate, or a fatty amine salt of an alkylaryl sulphonic acid, esp. sorbitan triolate. The carrier is calcium carbonate or a sugar, esp. lactose.

The amt. of antistatic agent is 0.01-2.0(esp. 0.1-0.5) wt.%. the cover of drug is 0.01-5.0(esp. 0.2-2.0)wt.%. The amt. of carrier is 95.0-99.99(esp. 48-.0-99.8) wt.%.

USE/ADVANTAGE - The compsns. are useful for delivery of active agent to the lungs and give reduced side effects, such as nausea, by maximising its proportion of drug reaching the lungs.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A12-V01; B01-B02; B04-C01; B04-J04A; B04-N02; B07-H; B10-B03B; B10-D02; B10-D03; **B12-M01B**; B12-M11G

ABEQ EP 654991 B UPAB: 19970709

A powder composition for inhalation comprising at one **microfine** drug and a carrier, in which at least a portion of the said carrier, but none of said drug, comprises an antistatic agent.

Dwg.0/0

L151 ANSWER 14 OF 38 WPIX (C) 2002 THOMSON DERWENT

AN 1994-007168 [01] WPIX

CR 1994-007163 [01]

DNC C1994-002782

TI **Ultrafine** powder for inhalation to be transferred to lower airway - comprises drug and hydroxypropyl cellulose and/or hydroxypropyl-methyl cellulose, exhibiting good stability and drug-releasing property.

DC A96 B07

IN KOBAYASHI, H; MAKINO, Y; SAKAGAMI, M; SAKON, K; SUZUKI, Y

PA (TEIJ) TEIJIN LTD

CYC 22

PI WO 9325198 A1 19931223 (199401)* JA 31p A61K009-72 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US

AU 9343556 A 19940104 (199417) A61K009-72 <--

JP 06500913 X 19940602 (199426) A61K009-72 <--

EP 611567 A1 19940824 (199433) EN 18p A61K009-72 <--
R: AT BE CH DE ES FR GB IT LI NL SE

AU 659328 B 19950511 (199527) A61K009-72 <--

EP 611567 A4 19961023 (199710) A61K009-72 <--
JP 2907551 B2 19990621 (199930) 11p A61K009-72 <--
US 5972388 A 19991026 (199952) A61K009-14 <--
CA 2115065 C 20001003 (200056) EN A61K009-72 <--
KR 277622 B 20010115 (200207) A61K009-72 <--

ADT WO 9325198 A1 WO 1993-JP786 19930611; AU 9343556 A AU 1993-43556 19930611; JP 06500913 X WO 1993-JP786 19930611, JP 1994-500913 19930611; EP 611567 A1 EP 1993-913510 19930611, WO 1993-JP786 19930611; AU 659328 B AU 1993-43556 19930611; EP 611567 A4 EP 1993-913510 ; JP 2907551 B2 WO 1993-JP786 19930611, JP 1994-500913 19930611; US 5972388 A Cont of WO 1993-JP786 19930611, Cont of US 1994-193181 19940214, US 1997-779614 19970107; CA 2115065 C CA 1993-2115065 19930611, WO 1993-JP786 19930611; KR 277622 B WO 1993-JP786 19930611, KR 1994-700408 19940208

FDT AU 9343556 A Based on WO 9325198; JP 06500913 X Based on WO 9325198; EP 611567 A1 Based on WO 9325198; AU 659328 B Previous Publ. AU 9343556, Based on WO 9325198; JP 2907551 B2 Based on WO 9325198; CA 2115065 C Based on WO 9325198; KR 277622 B Previous Publ. KR 94701660, Based on WO 9325198

PRAI **JP 1992-215133 19920812; JP 1992-153538 19920612**

REP EP 23359; EP 464171; GB 2240337; JP 04504427; JP 56020509; JP 57032215; US 4294829; WO 9111179; 1.Jnl.Ref; DE 2851489; EP 193372; EP 504760; GB 2193891; US 4462983; WO 9110434

IC ICM **A61K009-14; A61K009-72**
ICS **A61K009-12**; A61K009-19; A61K047-38

AB WO 9325198 A UPAB: 20020130

Ultrafine powder for inhalation comprises a drug and/or hydroxy-propyl cellulose and/or hydroxypropylmethyl cellulose. More than 80 wt.% particles in the powder have a particle dia. of 0.5-10 **microns.**

Prepn. of the powder is also claimed by spray-drying.

Pref. the drug can be steroid, anti-allergy drugs, drugs for bronchodilation, chemical therapeutic drugs for infections, cough drugs, anti-malignant tumour drugs, cardiovascular drugs, physiologically active peptide tampac and vaccines, etc. In the prepn. of the powder, a dispersing additive and/or diluent is used.

ADVANTAGE - The powder can reach lower wind pipe and bronchi and has good deposit properties. The powder that has deposited has good storage properties and can release drugs continuously. In addn., the powder is easy and safe to produce.

Dwg.0/5

FS CPI
FA AB; DCN
MC CPI: A03-A04A1; A12-V01; B01-B01; **B12-M01B**; B12-M11G; B14-K01A; B14-K01D

L151 ANSWER 15 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1993-272545 [34] WPIX
DNC C1993-121546
TI **Aerosol** formulations contg. **beclomethasone di propionate** mono hydrate - have specified water content for prolonged stability.
DC B01 P34
IN NEALE, P J; TAYLOR, A J; TAILOR, A J; JAMES, A
PA (GLAX) GLAXO GROUP LTD
CYC 47
PI WO 9315741 A1 19930819 (199334)* EN 18p A61K031-57 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US
AU 9334525 A 19930903 (199401) A61K031-57 <--
ZA 9300800 A 19940223 (199414) 17p A61K000-00 <--
NO 9402923 A 19940805 (199438) A61K031-57 <--
EP 625046 A1 19941123 (199445) EN A61K031-57 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

CZ 9401846	A3	19950315	(199520)		A61K009-12	<--
JP 07503476	W	19950413	(199523)		A61K031-57	<--
SK 9400924	A3	19950412	(199524)		A61K031-57	<--
HU 68986	T	19950828	(199540)		A61K031-57	<--
AU 667074	B	19960307	(199617)		A61K009-12	<--
NZ 246889	A	19961126	(199701)		A61K031-57	
CN 1078633	A	19931124	(199711)		A61K009-12	<--
CZ 281942	B6	19970416	(199722)		A61K009-12	<--
TW 299234	A	19970301	(199723)		A61K009-12	<--
EP 625046	B1	19970910	(199741) EN	14p	A61K031-57	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						
DE 69313825	E	19971016	(199747)		A61K031-57	
ES 2106360	T3	19971101	(199750)		A61K031-57	
US 5688782	A	19971118	(199801)	5p	A61K031-56	
US 5695744	A	19971209	(199804)	4p	A61L009-04	
SK 279291	B6	19980909	(199848)		A61K031-57	
IL 104628	A	19981227	(199907)		A61K031-57	
NO 306453	B1	19991108	(199953)		A61K031-57	
RU 2120285	C1	19981020	(200011)		A61K031-56	
MX 193240	B	19990903	(200067)		A61K031-057	

ADT WO 9315741 A1 WO 1993-EP223 19930202; AU 9334525 A AU 1993-34525 19930202; ZA 9300800 A ZA 1993-800 19930205; NO 9402923 A WO 1993-EP223 19930202, NO 1994-2923 19940805; EP 625046 A1 EP 1993-917355 19930202, WO 1993-EP223 19930202; CZ 9401846 A3 CZ 1994-1846 19930202; JP 07503476 W JP 1993-513729 19930202, WO 1993-EP223 19930202; SK 9400924 A3 WO 1993-EP223 19930202, SK 1994-924 19930202; HU 68986 T WO 1993-EP223 19930202, HU 1994-2301 19930202; AU 667074 B AU 1993-34525 19930202; NZ 246889 A NZ 1993-246889 19930202, WO 1993-EP223 19930202; CN 1078633 A CN 1993-102529 19930205; CZ 281942 B6 WO 1993-EP223 19930202, CZ 1994-1846 19930202; TW 299234 A TW 1993-100772 19930205; EP 625046 B1 EP 1993-917355 19930202, WO 1993-EP223 19930202; DE 69313825 E DE 1993-613825 19930202, EP 1993-917355 19930202, WO 1993-EP223 19930202; ES 2106360 T3 EP 1993-917355 19930202; US 5688782 A Div ex WO 1993-EP223 19930202, Div ex US 1994-256294 19940712, US 1995-458241 19950602; US 5695744 A WO 1993-EP223 19930202, US 1994-256294 19940712; SK 279291 B6 WO 1993-EP223 19930202, SK 1994-924 19930202; IL 104628 A IL 1993-104628 19930205; NO 306453 B1 WO 1993-EP223 19930202, NO 1994-2923 19940805; RU 2120285 C1 RU 1994-40361 19930202; MX 193240 B MX 1993-620 19930204

FDT AU 9334525 A Based on WO 9315741; EP 625046 A1 Based on WO 9315741; JP 07503476 W Based on WO 9315741; HU 68986 T Based on WO 9315741; AU 667074 B Previous Publ. AU 9334525, Based on WO 9315741; NZ 246889 A Based on WO 9315741; CZ 281942 B6 Previous Publ. CZ 9401846; EP 625046 B1 Based on WO 9315741; DE 69313825 E Based on EP 625046, Based on WO 9315741; ES 2106360 T3 Based on EP 625046; US 5695744 A Based on WO 9315741; SK 279291 B6 Previous Publ. SK 9400924; NO 306453 B1 Previous Publ. NO 9402923

PRAI **GB 1992-2519 19920206**

REP GB 2076422; GB 2107715; WO 9206675

IC ICM A61K000-00; **A61K009-12**; A61K031-057; A61K031-56; A61K031-57; A61L009-04
ICS A61K009-00; A61K009-012; **A61K009-72**

ICA C07J009-00

AB WO 9315741 A UPAB: 19980112
Compsn. comprises (by wt): a) **beclomethasone dipropionate** monohydrate (pref. 0.005-10%) of particle size substantially less than 20 **microns** alone or in combination with salbutamol or salmeterol xinafoate; (b) at least 0.015% pref. 0.026-0.08% of the formulation of water in addition to the water of **crystallisation** assoc. with said monohydrate and c) a fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant (pref. 1,1,1,2,3,3,3-hepafluoro -n-propane or 1,1,1,2-tetrafluoroethane).
USE/ADVANTAGE - The formulations are stable and the particle size does not increase on staorage due to solvates formulating so that the medicament particles do not become too large to penetrate the lungs. Daily

doses of **beclomethasone dipropionate** are in the range (100-2000mcg given by filled canisters and metered dose inhalers, 1-4 puffs, 1-8 times per day
Dwg.0/0
FS CPI GMPI
FA AB; DCN
MC CPI: B01-B02; B10-E04C; B10-H02B; B10-H02F; B11-C03; B12-A02C; B12-K06; **B12-M01A; B12-M01B**
ABEQ EP 625046 B UPAB: 19971013
A pharmaceutical **aerosol** formulation which comprises: (a) particulate **beclomethasone dipropionate** monohydrate, the particle size of substantially all the monohydrate being less than 20 **microns**; (b) at least 0.015% by weight of the formulation is water in addition to the water of **crystallisation** associated with the monohydrate; and (c) a fluorocarbon or hydrogen-containing chlorofluorocarbon propellant.
Dwg.0/0
ABEQ US 5688782 A UPAB: 19980107
Compsn. comprises (by wt): a) **beclomethasone dipropionate** monohydrate (pref. 0.005-10%) of particle size substantially less than 20 **microns** alone or in combination with salbutamol or salmeterol xinafoate; (b) at least 0.015% pref. 0.026-0.08% of the formulation of water in addition to the water of **crystallisation** assoc. with said monohydrate and c) a fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant (pref. 1,1,1,2,3,3,3-hepafluoro -n-propane or 1,1,1,2-tetrafluoroethane).
USE/ADVANTAGE - The formulations are stable and the particle size does not increase on storage due to solvates formulating so that the medicament particles do not become too large to penetrate the lungs. Daily doses of **beclomethasone dipropionate** are in the range (100-2000mcg given by filled canisters and metered dose inhalers, 1-4 puffs, 1-8 times per day.
Dwg.0/0
ABEQ US 5695744 A UPAB: 19980126
Compsn. comprises (by wt): a) **beclomethasone dipropionate** monohydrate (pref. 0.005-10%) of particle size substantially less than 20 **microns** alone or in combination with salbutamol or salmeterol xinafoate; (b) at least 0.015% pref. 0.026-0.08% of the formulation of water in addition to the water of **crystallisation** assoc. with said monohydrate and c) a fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant (pref. 1,1,1,2,3,3,3-hepafluoro -n-propane or 1,1,1,2-tetrafluoroethane).
USE/ADVANTAGE - The formulations are stable and the particle size does not increase on staorage due to solvates formulating so that the medicament particles do not become too large to penetrate the lungs. Daily doses of **beclomethasone dipropionate** are in the range (100-2000mcg given by filled canisters and metered dose inhalers, 1-4 puffs, 1-8 times per day
Dwg.0/0

L151 ANSWER 16 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1993-213782 [26] WPIX
DNC C1993-094785
TI Suspension formulation for **aerosol** admin. - comprising drug and 1,1,1,2-tetra fluoroethane or 1,1,1,2,3,3,3-hepta fluoro propane as propellant.
DC B07
IN JINKS, P A; MORIS, R A; OLIVER, M J; SCHULTZ, D W; SCHULTZ, R K; MORRIS, R A
PA (MINN) MINNESOTA MINING & MFG CO
CYC 21
PI WO 9311747 A1 19930624 (199326)* EN 38p A61K009-00 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

W: AU CA JP NZ
AU 9332728 A 19930719 (199344) A61K009-00 <--
EP 617610 A1 19941005 (199438) EN A61K009-00 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 07502275 W 19950309 (199518) A61K009-12 <--
NZ 246421 A 19960528 (199626) A61K009-12 <--
EP 717987 A2 19960626 (199630) EN 8p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 717987 A3 19960703 (199636) A61K009-00
AU 675633 B 19970213 (199715) A61K009-12 <--
EP 617610 B1 19970319 (199716) EN 12p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 9712342 A 19970320 (199720) A61K009-12 <--
DE 69218455 E 19970424 (199722) A61K009-00
ES 2099415 T3 19970516 (199727) A61K009-00
AU 709052 B 19990819 (199945) A61K009-12 <--
CA 2126244 C 20000926 (200055) EN A61K009-12 <--
CA 2320129 A1 19930624 (200067) EN A61K009-12 <--
EP 1086688 A1 20010328 (200118) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 717987 B1 20010829 (200150) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69232034 E 20011004 (200166) A61K009-00
ES 2159678 T3 20011016 (200173) A61K009-00

ADT WO 9311747 A1 WO 1992-US10587 19921211; AU 9332728 A AU 1993-32728 19921211; EP 617610 A1 WO 1992-US10587 19921211, EP 1993-901414 19921211; JP 07502275 W WO 1992-US10587 19921211, JP 1993-511027 19921211; NZ 246421 A NZ 1992-246421 19921211, WO 1992-US10587 19921211; EP 717987 A2 Div ex EP 1993-901414 19921211, EP 1996-200109 19921211; EP 717987 A3 Div ex EP 1993-901414 19921211, EP 1996-200109 19921211; AU 675633 B AU 1993-32728 19921211; EP 617610 B1 WO 1992-US10587 19921211, EP 1993-901414 19921211; AU 9712342 A Div ex AU 1993-32728 19921211, AU 1997-12342 19970128; DE 69218455 E DE 1992-618455 19921211, WO 1992-US10587 19921211, EP 1993-901414 19921211; ES 2099415 T3 EP 1993-901414 19921211; AU 709052 B Div ex AU 1993-32728 19921211, AU 1997-12342 19970128; CA 2126244 C CA 1992-2126244 19921211, WO 1992-US10587 19921211; CA 2320129 A1 Div ex CA 1992-2126244 19921211, CA 1992-2320129 19921211; EP 1086688 A1 Div ex EP 1993-901414 19921211, Div ex EP 1996-200109 19921211, EP 2000-123885 19921211; EP 717987 B1 Div ex EP 1993-901414 19921211, EP 1996-200109 19921211, Related to EP 2000-123885 19921211; DE 69232034 E DE 1992-632034 19921211, EP 1996-200109 19921211; ES 2159678 T3 EP 1996-200109 19921211

FDT AU 9332728 A Based on WO 9311747; EP 617610 A1 Based on WO 9311747; JP 07502275 W Based on WO 9311747; NZ 246421 A Based on WO 9311747; AU 675633 B Previous Publ. AU 9332728, Based on WO 9311747; EP 617610 B1 Based on WO 9311747; DE 69218455 E Based on EP 617610, Based on WO 9311747; ES 2099415 T3 Based on EP 617610; AU 709052 B Div ex AU 675633, Previous Publ. AU 9712342; CA 2126244 C Based on WO 9311747; EP 1086688 A1 Div ex EP 617610, Div ex EP 717987; EP 717987 B1 Related to EP 1086688, Div ex EP 617610; DE 69232034 E Based on EP 717987; ES 2159678 T3 Based on EP 717987

PRAI **US 1991-809791 19911218; US 1991-810401 19911218 ; US 1992-878039 19920504**

REP EP 372777; WO 9104011; WO 9111495; WO 9208446; No-SR.Pub

IC **A61K009-12**
ICM A61K009-00; **A61K009-12**
ICS **A61K009-72**; A61K031-135; A61K031-137; A61K031-16; A61K031-44; A61M011-08

AB WO 9311747 A UPAB: 19931116
(A) A pharmaceutical suspension formulation suitable for **aerosol** admin. is claimed consisting of a drug and a propellant selected from HFC 134a (1,1,1,2-tetrafluoroethane) and HFC 227 (1,1,1,2,3,3,3-heptafluoropropane, the formulation being characterised in that it exhibits no growth in particle size or change in **crystal** morphology of the drug over a prolonged priod, is readily redispersible

and upon redispersion does not flocculate so quickly as to prevent reproducible dosing of the drug.

The drug may be eg. formoterol, salmeterol, albuterol, **beclomethasone dipropionate**, cromolyn or pirbuterol.

Also claimed are: (B) a suspension **aerosol** formulation comprising a **micronised** drug selected from pirbuterol acetate and pirbuterol. HCl and a propellant comprising HFC227, the formulation being further characterised in that it is free of perfluorinated **surfactant**. (C) a suspension **aerosol** formulation comprising **micronised** albuterol sulphate and HFC 227 as the only propellant.

USE/ADVANTAGE - The formulations can provide a reproducible dose of drug for **aerosol** admin. They can be delivered to the lung by oral inhalation to treat eg. asthma or chronic obstructive pulmonary disease. They can also be delivered by nasal inhalation to treat eg. allergic rhinitis, rhinites or diabetes or can be delivered by topical (eg buccal) admin. to treat eg. angina or local infection.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B07-D04C; B10-B03B; B10-H02B; B12-A01; B12-D02; B12-F02; B12-G03; B12-K02; B12-K06; B12-L04; **B12-M01A**

ABEQ EP 617610 B UPAB: 19970417

A pharmaceutical suspension formulation suitable for **aerosol** administration, consisting of a therapeutically effective amount of a drug and a propellant selected from HFC 134a, HFC 227 and a mixture thereof, the formulation exhibiting substantially no growth in particle size or change in **crystal** morphology of the drug over a prolonged period, being substantially and readily redispersible, and upon redispersion does not flocculate so quickly as to prevent reproducible dosing of the drug.

Dwg.0/0

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AN 1993-213781 [26] WPIX

CR 1993-213779 [26]; 1993-213780 [26]

DNC C1993-094784

TI **Aerosol** formulation for pharmaceutical admin. by inhalation - contg particulate medicament, hydrogen contg. chloro-fluoro-carbon propellant and polar co-solvent, for antiallergics, bronchodilators, and antiinflammatories.

DC B05 B07 P34

IN AKEHURST, R A; TAYLOR, A J; WYATT, D A

PA (GLAX) GLAXO GROUP LTD

CYC 43

PI	WO 9311745	A1	19930624 (199326)*	EN	24p	A61K009-00	<--
	RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE						
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	AU 9230852	A	19930719 (199344)				<--
	ZA 9209618	A	19930929 (199344)		21p	A61K000-00	<--
	EP 616525	A1	19940928 (199437)	EN			<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						
	TW 229159	A	19940901 (199439)			A61K047-06	<--
	JP 07501811	W	19950223 (199517)			A61K009-12	<--
	EP 616525	B1	19950927 (199543)	EN	13p		<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						
	DE 69205177	E	19951102 (199549)				<--
	AU 663906	B	19951026 (199550)			A61K009-12	<--
	NZ 246046	A	19951221 (199606)			A61K009-12	<--
	ES 2079210	T3	19960101 (199608)				
	US 5736124	A	19980407 (199821)		7p	A61K009-12	<--
	US 5817293	A	19981006 (199847)			A61K009-12	<--

US 5916540	A	19990629	(199932)		A61K009-12	<--
MX 190305	B	19981111	(200043)		A01N043-000	
US 6221339	B1	20010424	(200125)		A61K009-14	<--
CA 2125665	C	20010612	(200136)	EN	A61K009-12	<--
US 6333023	B1	20011225	(200206)		A61K009-12	<--
US 2002058011	A1	20020516	(200237)		A61L009-04	

ADT WO 9311745 A1 WO 1992-EP2810 19921204; AU 9230852 A AU 1992-30852 19921204; ZA 9209618 A ZA 1992-9618 19921211; EP 616525 A1 EP 1992-924669 19921204, WO 1992-EP2810 19921204; TW 229159 A TW 1992-110011 19921214; JP 07501811 W WO 1992-EP2810 19921204, JP 1993-510575 19921204; EP 616525 B1 EP 1992-924669 19921204, WO 1992-EP2810 19921204; DE 69205177 E DE 1992-605177 19921204, EP 1992-924669 19921204, WO 1992-EP2810 19921204; AU 663906 B AU 1992-30852 19921204; NZ 246046 A NZ 1992-246046 19921204; ES 2079210 T3 EP 1992-924669 19921204; US 5736124 A Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Cont of US 1994-328957 19941024, US 1995-453820 19950530; US 5817293 A Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Div ex US 1994-328957 19941024, US 1995-453760 19950530; US 5916540 A Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Cont of US 1994-328957 19941024, Cont of US 1995-453820 19950530, US 1998-55253 19980406; MX 190305 B MX 1992-7200 19921211; US 6221339 B1 Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Cont of US 1994-328957 19941024, Cont of US 1995-453820 19950530, Cont of US 1998-55253 19980406, US 1999-307552 19990510; CA 2125665 C CA 1992-2125665 19921204, WO 1992-EP2810 19921204; US 6333023 B1 Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Cont of US 1994-328957 19941024, Cont of US 1995-453820 19950530, Cont of US 1998-55253 19980406, Cont of US 1999-307552 19990510, US 2000-562098 20000501; US 2002058011 A1 Cont of WO 1992-EP2810 19921204, Cont of US 1993-94174 19930805, Cont of US 1994-328957 19941024, Cont of US 1995-453820 19950530, Cont of US 1998-55253 19980406, Cont of US 1999-307552 19990510, Cont of US 2000-562098 20000501, US 2001-986272 20011108

FDT AU 9230852 A Based on WO 9311745; EP 616525 A1 Based on WO 9311745; JP 07501811 W Based on WO 9311745; EP 616525 B1 Based on WO 9311745; DE 69205177 E Based on EP 616525, Based on WO 9311745; AU 663906 B Previous Publ. AU 9230852, Based on WO 9311745; ES 2079210 T3 Based on EP 616525; US 5916540 A Cont of US 5736124; US 6221339 B1 Cont of US 5736124, Cont of US 5916540; CA 2125665 C Based on WO 9311745; US 6333023 B1 Cont of US 5736124, Cont of US 5916540, Cont of US 6221339; US 2002058011 A1 Cont of US 5736124, Cont of US 5916540, Cont of US 6221339

PRAI **GB 1992-2522 19920206; GB 1991-26444 19911212**

REP EP 372777; EP 504112; WO 8604233; WO 9208446

IC ICM A01N043-000; A61K000-00; A61K009-00; **A61K009-12**; **A61K009-14**; A61K047-06; A61L009-04

ICS A01N025-004; A01N025-030; A01N047-030; **A61K009-72**; A61K031-045; A61K031-135; A61K031-35; A61K031-56; A61K031-57

AB WO 9311745 A UPAB: 20020613

The formulation comprises particulate medicament, a (hydrogen-contg. chloro) fluorocarbon propellant and up to 5% w/w wrt propellant of a polar cosolvent and the formulation is free of a **surfactant**.

Pref a metered dose inhaler comprises the canister delivering compsn fitted into a pref channelling device.

The medicament may be pref an antiallergic, a bronchodilator or an antiinflammatory steroid eg. salmeterol, salbutamol, fluticasone propionate, **beclomethasone dipropionate** and salts. The formulation may contain medicaments. The particle size of the particulate medicament is pref less than 100 **microns**. (1-10 **microns**) esp. 1-5 **microns**.

USE/ADVANTAGE - The formulations are used for the admin. of medicaments by inhalation. Medicines administered are eg analgesics, anginal prepns., antiallergics, antiinfectives, antihistamines, antiinflammatories, antitussives, bronchodilators, diuretics, anticholinergics, hormones, xanthines and therapeutic proteins or

peptides. The formulation is partic useful in the treatment of asthma.
The formulation is free, i.e. not more than 0.0001% by wt. of **surfactant**.
Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: B04-B02D; B11-C09; B12-D02; B12-D07; B12-K02; **B12-M01A**
ABEQ ZA 9209618 A UPAB: 19931213
Aerosol formulations of use for the admin. of medicaments by inhalation, in particular a pharmaceutical **aerosol** formulation, comprises particulate medicament, fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant and up to 5% w/w based upon propellant of a polar cosolvent, which formulation is substantially free of **surfactant**. Treating respiratory disorders comprises administration by inhalation an effective amt. of a pharmaceutical **aerosol** formulation.
ABEQ EP 616525 B UPAB: 19951102
A pharmaceutical **aerosol** formulation which comprises particulate medicament, a fluorocarbon or hydrogen-containing chlorofluorocarbon propellant and 0.01 to 5% w/w based upon propellant of polar cosolvent, which formulation is substantially free of **surfactant**.
Dwg.0/0

L151 ANSWER 18 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1993-213779 [26] WPIX
CR 1993-213780 [26]; 1993-213781 [26]
DNC C1993-094782
TI **Surfactant** free **aerosol** formulation for treatment of e.g. asthma - uses ozone-friendly fluorocarbon or hydrogen contg. chloro-fluorocarbon propellant.
DC B05 B07 P33 P34 Q34
IN AKEHURST, R A; TAYLOR, A J; WYATT, D A; MARRIOTT, R A; WYTATT, D A
PA (GLAX) GLAXO GROUP LTD
CYC 48
PI WO 9311743 A1 19930624 (199326)* EN 22p A61K009-00 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO NZ PL PT RO RU SD SE US
AU 9230850 A 19930719 (199344) A61K009-00 <--
CN 1075078 A 19930811 (199419) A61K009-12 <--
CN 1075079 A 19930811 (199419) A61K009-12 <--
ZA 9209617 A 19940525 (199423) 21p A61K000-00 <--
NO 9402185 A 19940610 (199430) A61K009-12 <--
EP 616523 A1 19940928 (199437) EN A61K009-00 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
TW 229159 A 19940901 (199439) A61K047-06 <--
TW 232654 A 19941021 (199501) A61K047-06 <--
JP 07502033 W 19950302 (199517) A61K031-02 <--
CZ 9401430 A3 19950315 (199520) A61K009-12 <--
SK 9400674 A3 19950308 (199520) A61K009-00 <--
HU 67534 T 19950428 (199523) A61K009-72 <--
AU 663904 B 19951026 (199550) A61K009-12 <--
NZ 246046 A 19951221 (199606) A61K009-12 <--
NZ 246044 A 19960126 (199610) A61K009-12 <--
EP 756868 A2 19970205 (199711) EN 11p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 756868 A3 19970226 (199717) A61K009-00
US 5653962 A 19970805 (199737) 7p A61K009-12 <--
US 5658549 A 19970819 (199739) 9p A61K009-12 <--
US 5674471 A 19971007 (199746) 8p A61K009-12 <--
US 5674472 A 19971007 (199746) 7p A61K009-12 <--
US 5676929 A 19971014 (199747) 7p A61K009-12 <--
US 5683676 A 19971104 (199750) 7p A61K009-12 <--

EP 616523 B1 19980304 (199813) EN 16p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69224656 E 19980409 (199820) A61K009-00
BR 1100355 A3 19980414 (199821) A61K009-12 <--
ES 2113444 T3 19980501 (199824) A61K009-00
IL 104068 A 19981030 (199905) A61K009-12 <--
SK 279920 B6 19990507 (199926) A61K009-12 <--
SG 55800 A1 19990118 (199930) A61K009-00
US 5922306 A 19990713 (199934) A61K009-12 <--
JP 11310533 A 19991109 (200004) 6p A61K031-57
BR 1101178 A3 19991207 (200015) A61K009-12 <--
JP 3026840 B2 20000327 (200020) 8p A61K031-137
JP 3026841 B2 20000327 (200020) 6p A61K031-137
EP 990437 A1 20000405 (200021) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
RU 2129424 C1 19990427 (200025) A61K009-12 <--
NO 2000001227 A 19940610 (200032) A61K009-12 <--
NO 307864 B1 20000613 (200035) A61K009-12 <--
CA 2303685 A1 19930624 (200041) EN A61K009-12 <--
CA 2125667 C 20000613 (200042) EN A61K009-12 <--
MX 190268 B 19981109 (200043) A61K009-012
MX 190305 B 19981111 (200043) A01N043-000
CZ 287039 B6 20000816 (200048) A61K009-12 <--
SG 74042 A1 20000718 (200051) A61K009-00
EP 1066828 A1 20010110 (200103) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 6200549 B1 20010313 (200120) A61K009-12 <--
CN 1284330 A 20010221 (200131) A61K009-12 <--
EP 756868 B1 20010530 (200131) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 6238647 B1 20010529 (200132) A61K009-02
US 6251368 B1 20010626 (200138) A61K009-12 <--
DE 69231857 E 20010705 (200146) A61K009-00
ES 2158988 T3 20010916 (200164) A61K009-00
US 6303103 B1 20011016 (200164) A61K009-12 <--
KR 278339 B 20010115 (200207) A61K009-12 <--
CA 2362539 A1 19930624 (200213) EN A61K031-57 <--
CA 2303685 C 20020212 (200221) EN A61K009-12 <--
US 2002028183 A1 20020307 (200221) A61L009-04
US 2002031479 A1 20020314 (200222) A61K009-00
RU 2179037 C2 20020210 (200228) A61M015-00
JP 3280974 B2 20020513 (200234) 11p A61K009-12 <--

ADT WO 9311743 A1 WO 1992-EP2808 19921204; AU 9230850 A AU 1992-30850 19921204; CN 1075078 A CN 1993-100476 19930102; CN 1075079 A CN 1993-100477 19930102; ZA 9209617 A ZA 1992-9617 19921211; NO 9402185 A WO 1992-EP2808 19921204, NO 1994-2185 19940610; EP 616523 A1 EP 1992-924667 19921204, WO 1992-EP2808 19921204; TW 229159 A TW 1992-110011 19921214; TW 232654 A TW 1992-110012 19921214; JP 07502033 W WO 1992-EP2808 19921204, JP 1993-510573 19921204; CZ 9401430 A3 CZ 1994-1430 19921204; SK 9400674 A3 SK 1994-674 19940603, WO 1992-EP2808 ; HU 67534 T WO 1992-EP2808 19921204, HU 1994-1742 19921204; AU 663904 B AU 1992-30850 19921204; NZ 246046 A NZ 1992-246046 19921204; NZ 246044 A NZ 1992-246044 19921204; EP 756868 A2 Div ex EP 1992-924667 19921204, EP 1996-202592 19921204; EP 756868 A3 Div ex EP 1992-924667 19921204, EP 1996-202592 19921204; US 5653962 A Div ex WO 1992-EP2808 19921204, Cont of US 1993-102241 19930805, Cont of US 1994-328959 19941024, US 1995-444928 19950519; US 5658549 A Div ex WO 1992-EP2808 19921204, Cont of US 1993-102235 19930805, Cont of US 1994-328960 19941024, US 1995-444925 19950519; US 5674471 A Div ex WO 1992-EP2808 19921204, Cont of US 1993-102237 19930805, Cont of US 1994-328958 19941024, US 1995-444725 19950519; US 5674472 A Div ex WO 1992-EP2808 19921204, Cont of US 1993-102235 19930805, Div ex US 1994-328960 19941024, US 1995-444919 19950519; US 5676929 A Div ex WO 1992-EP2808 19921204, Cont of US

1993-102237 19930805, Div ex US 1994-328958 19941024, US 1995-444743 19950519; US 5683676 A Div ex WO 1992-EP2808 19921204, Cont of US 1993-102241 19930805, Div ex US 1994-328959 19941024, US 1995-444926 19950519; EP 616523 B1 EP 1992-924667 19921204, WO 1992-EP2808 19921204, Related to EP 1996-202592 19921204; DE 69224656 E DE 1992-624656 19921204, EP 1992-924667 19921204, WO 1992-EP2808 19921204; BR 1100355 A3 BR 1997-1100355 19970428; ES 2113444 T3 EP 1992-924667 19921204; IL 104068 A IL 1992-104068 19921211; SK 279920 B6 WO 1992-EP2808 19921204, SK 1994-674 19921204; SG 55800 A1 SG 1996-7893 19921204; US 5922306 A Cont of WO 1992-EP2809 19921204, Cont of US 1993-94175 19930805, Cont of US 1994-302435 19940909, Cont of US 1995-462558 19950605, US 1998-60110 19980415; JP 11310533 A Div ex JP 1993-510573 19921204, JP 1999-64667 19921204; BR 1101178 A3 BR 1997-1101178 19970428; JP 3026840 B2 WO 1992-EP2808 19921204, JP 1993-510573 19921204; JP 3026841 B2 WO 1992-EP2809 19921204, JP 1993-510574 19921204; EP 990437 A1 Div ex EP 1992-924667 19921204, Div ex EP 1996-202592 19921204, EP 1999-204248 19921204; RU 2129424 C1 WO 1992-EP2808 19921204, RU 1994-30722 19921204; NO 2000001227 A WO 1992-EP2808 19921204, Div ex NO 1994-2185 19940610, NO 2000-1227 20000309; NO 307864 B1 WO 1992-EP2808 19921204, NO 1994-2185 19940610; CA 2303685 A1 Div ex CA 1992-2125667 19921204, CA 1992-2303685 19921204; CA 2125667 C CA 1992-2125667 19921204, WO 1992-EP2808 19921204; MX 190268 B MX 1992-7205 19921211; MX 190305 B MX 1992-7200 19921211; CZ 287039 B6 WO 1992-EP2808 19921204, CZ 1994-1430 19921204; SG 74042 A1 SG 1998-284 19921204; EP 1066828 A1 Div ex EP 1996-202592 19921204, Div ex EP 1999-204248 19921204, EP 2000-202961 19921204; US 6200549 B1 Cont of WO 1992-EP2809 19921204, Cont of US 1993-94175 19930805, Cont of US 1994-302435 19940909, Cont of US 1995-462558 19950605, Cont of US 1998-60110 19980415, US 1999-264665 19990309; CN 1284330 A Div ex CN 1993-100476 19930112, CN 2000-120072 19930112; EP 756868 B1 Div ex EP 1992-924667 19921204, EP 1996-202592 19921204, Related to EP 1999-204248 19921204; US 6238647 B1 Div ex WO 1992-EP2808 19921204, Cont of US 1993-102237 19930805, Div ex US 1994-328958 19941024, Div ex US 1995-444743 19950519, Cont of US 1997-877198 19970617, US 1999-431872 19991102; US 6251368 B1 Div ex WO 1992-EP2808 19921204, Cont of US 1993-102237 19930805, Div ex US 1994-328958 19941024, Div ex US 1995-444743 19950519, US 1997-877198 19970617; DE 69231857 E DE 1992-631857 19921204, EP 1996-202592 19921204; ES 2158988 T3 EP 1996-202592 19921204; US 6303103 B1 Div ex WO 1992-EP2808 19921204, Cont of US 1993-102237 19930805, Div ex US 1994-328958 19941024, Div ex US 1995-444743 19950519, Cont of US 1997-877198 19970617, Cont of US 1999-431923 19991102, US 2000-593380 20000614; KR 278339 B WO 1992-EP2808 19921204, KR 1994-702000 19940611; CA 2362539 A1 Div ex CA 1992-2303685 19921204, CA 1992-2362539 19921204; CA 2303685 C Div ex CA 1992-2125667 19921204, CA 1992-2303685 19921204; US 2002028183 A1 Div ex WO 1992-EP2810 19921204, Cont of US 1993-102237 19930805, Div ex US 1994-328958 19941024, Div ex US 1995-444743 19950519, Cont of US 1997-877198 19970617, US 2001-885133 20010621; US 2002031479 A1 Cont of WO 1992-EP2809 19921204, Cont of US 1993-94175 19930805, Cont of US 1994-302435 19940909, Cont of US 1995-462558 19950605, Cont of US 1998-60110 19980415, Cont of US 1999-264665 19990309, Cont of US 2000-559574 20000428, US 2001-944213 20010904; RU 2179037 C2 Div ex RU 1994-30722 19921204, RU 1998-118908 19921204; JP 3280974 B2 WO 1992-EP2810 19921204, JP 1993-510575 19921204

FDT AU 9230850 A Based on WO 9311743; EP 616523 A1 Based on WO 9311743; JP 07502033 W Based on WO 9311743; HU 67534 T Based on WO 9311743; AU 663904 B Previous Publ. AU 9230850, Based on WO 9311743; EP 616523 B1 Related to EP 756868, Based on WO 9311743; DE 69224656 E Based on EP 616523, Based on WO 9311743; ES 2113444 T3 Based on EP 616523; SK 279920 B6 Previous Publ. SK 9400674; US 5922306 A Cont of US 5744123; JP 3026840 B2 Previous Publ. JP 07502033, Based on WO 9311743; JP 3026841 B2 Previous Publ. JP 07502034, Based on WO 9311744; EP 990437 A1 Div ex EP 616523, Div ex EP 756868; RU 2129424 C1 Based on WO 9311743; NO 307864 B1 Previous Publ. NO 9402185; CA 2125667 C Based on WO 9311743; CZ 287039 B6 Previous Publ. CZ 9401430, Based on WO 9311743; EP 1066828 A1 Div ex EP 756868, Div ex EP

990437; US 6200549 B1 Cont of US 5744123, Cont of US 5922306; EP 756868 B1 Div ex EP 616523, Related to EP 990437; US 6238647 B1 Div ex US 5676929; US 6251368 B1 Div ex US 5676929; DE 69231857 E Based on EP 756868; ES 2158988 T3 Based on EP 756868; US 6303103 B1 Div ex US 5676929; KR 278339 B Previous Publ. KR 94703176, Based on WO 9311743; US 2002028183 A1 Div ex US 5676929, Cont of US 6251368; US 2002031479 A1 Cont of US 5744123, Cont of US 5922306, Cont of US 6200549, Cont of US 6306369; JP 3280974 B2 Previous Publ. JP 07501811, Based on WO 9311745

PRAI **GB 1992-2522 19920206; GB 1991-26378 19911212 ; GB 1991-26405 19911212; GB 1991-26444 19911212**

REP WO 9111173; WO 9111496; WO 9208447; No-SR.Pub

IC ICM A01N043-000; A61K000-00; A61K009-00; A61K009-012; A61K009-02; **A61K009-12; A61K009-72**; A61K031-02; A61K031-137; A61K031-57; A61K047-06; A61L009-04; A61M015-00

ICS A01N025-004; A01N025-02; A01N025-030; A01N047-030; A61J001-00; **A61K009-14**; A61K031-00; A61K031-13; A61K031-135; A61K031-165; A61K031-352; A61K031-44; A61K031-522; A61K031-56; A61K031-573; A61K047-02; A61P011-00; A61P011-02; A61P011-08; A61P029-00; B65D083-14

ICA C07C217-10; C07J007-00; C07J031-00

AB WO 9311743 A UPAB: 20020610

Formulation comprises a particulate medicament (I) e.g. salmeterol, salbutamol, fluticasone propionate, becolomethasone **dipropionate** and a fluorocarbon or hydrogen-contg chlorofluorocarbon propellant.

Also claimed are the prepn of the **surface-modified** medicament and a canister for delivering metered doses of the **aerosol** formulation.

Pref., (I) is salmeterol xinafoate (Ia); salbutamol sulphate; fluticascone propionate; **beclomethasone dipropionate**; or a combination of salmeterol xinafoate and fluticasone propionate; or salbutamol and **beclomethasone dipropionate**. The propellant is pref. 1,1,1,2-tetrafluoroethane (II). (I) is present in an amt. of 0.005-10% wt. based on the total wt. of the formulation e.g. a salbutamol salt and 1,1,1,2-tetrafluoroethane in a ratio of 0.05:18 by wt. **Surface-modified** (I) are prepd. by admixture of particulate (I) with a non-polar, non-solvent liq. followed by removal of the lid.

USE/ADVANTAGE - The **aerosol** formulations are 'ozone friendly' using H-contg. chlorofluorocarbons as propellants and having no requirement for added **surfactants** or solvents for stabilising the constituent medicament(s). (I) can be used separately or in combination and may be e.g. analgesics, antiallergics, anti-infectives, antihistamines, anti-inflammatories, bronchodilators, diueretics, hormones, or therapeutic proteins and peptides. Admin. is by inhalation. Dosage of (I) is 50-2000 **micro**-g per day.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: B01-B02; B01-B03; B10-B03B; B10-H02B; B12-D01; B12-D02; B12-D06; B12-D07; B12-G03; B12-K02; **B12-M01A**

ABEQ EP 616525 B UPAB: 19951102

A pharmaceutical **aerosol** formulation which comprises particulate medicament, a fluorocarbon or hydrogen-containing chlorofluorocarbon propellant and 0.01 to 5% w/w based upon propellant of polar cosolvent, which formulation is substantially free of **surfactant**.

Dwg.0/0

ABEQ US 5653962 A UPAB: 19970915

A pharmaceutical **aerosol** formulation consisting essentially of a particulate medicament which is salmeterol or its salt or solvate and 1,1,1,2-tetrafluoroethane as propellant, which formulation contains less than 0.0001% w/w **surfactant** based upon the weight of medicament, the particulate medicament being present in an amount of from 0.005 to 5%

w/w relative to the total weight of the formulation and having a particle size of less than 100 **microns**.
Dwg.0/0

ABEQ US 5658549 A UPAB: 19970926
A pharmaceutical **aerosol** formulation consisting essentially of particulate medicament which is fluticasone propionate or a physiologically acceptable solvate thereof, and 1,1,1,2-tetrafluoroethane as propellant, which formulation contains less than 0.0001% w/w **surfactant** based upon the weight of medicament, the particulate medicament being present in an amount from 0.005% to 5% w/w relative to the total weight of the formulation and having a particle size of less than 100 **microns**.
Dwg.0/0

ABEQ US 5674471 A UPAB: 19971119
A pharmaceutical **aerosol** formulation consisting essentially of a particulate medicament which is salbutamol or a physiologically acceptable salt or solvate thereof and 1,1,1,2-tetrafluoroethane as propellant, which formulation contains less than 0.0001% **surfactant** based upon the weight of medicament, the particulate medicament being present in an amount of 0.005% to 5% w/w relative to the total weight of the formulation and having a particle size of less than 100 **microns**, with the provisos that when said formulation consists of salbutamol and 1,1,1,2-tetrafluoroethane in a weight ratio of 0.05:18, said salbutamol is present in the form of a physiologically acceptable salt and when said formulation consists of salbutamol or salbutamol sulphate and 1,1,1,2-tetrafluoroethane the weight to weight ratio of medicament to propellant is other than 69:7900 or 0.866%.
Dwg.0/0

ABEQ US 5674472 A UPAB: 19971119
A canister suitable for delivering a pharmaceutical **aerosol** formulation which comprises a container capable of withstanding the vapor pressure of the propellant used, which container is closed with a metering valve and contains a pharmaceutical **aerosol** formulation consisting essentially of a particulate medicament which is fluticasone propionate or a physiologically acceptable solvate thereof and 1,1,1,2-tetrafluoroethane as propellant. The formulation contains less than 0.0001% w/w **surfactant** based on the weight of the medicament, the particulate medicament being present in an amount 0.005-5% w/w relative to the total weight of the formulation and having a particle size of less than 100 **microns**.
Dwg.0/0

ABEQ US 5676929 A UPAB: 19971125
A canister suitable for delivering a pharmaceutical **aerosol** formulation for inhalation therapy which comprises a container capable of withstanding the vapor pressure of the propellant used, which container is a plastics-coated aluminum can and is closed with a metering valve and contains a pharmaceutical **aerosol** formulation consisting essentially of a particulate medicament which is salbutamol sulphate and 1,1,1,2-tetrafluoroethane as propellant, which formulation contains less than 0.0001% w/w **surfactant** based upon the weight of salbutamol sulphate, the particulate medicament being present in an amount of 0.01% to 1% w/w relative to the total weight of the formulation and having a particle size of less than 100 **microns**, and with the provisos than when said formulation consists of salbutamol and 1,1,1,2-tetrafluoroethane in a weight ratio of 0.05:18, said salbutamol is present in the form of a physiologically acceptable salt and that when said formulation consists of salbutamol or salbutamol sulphate and 1,1,1,2-tetrafluoroethane the weight to weight ratio of medicament to propellant is other than 69:7900 or 0.866%.
Dwg.0/0

ABEQ US 5683676 A UPAB: 19971217
A canister suitable for delivering a pharmaceutical **aerosol** formulation for inhalation therapy comprises a container capable of

withstanding the vapor pressure of the propellant. The container is closed with a metering valve and contains a pharmaceutical **aerosol** formulation consisting essentially of a particulate medicament which is salmeterol, a physiologically acceptable salt or their solvent, and 1,1,1,2-tetrafluoroethane as propellant. The formulation of the propellant contains < 0.0001% weight/weight **surfactant** based upon the weight of medicament. The particulate medicament is present in an amount of 0.005 to 5% weight/weight relative to the total weight of the formulation and having a particle size of < 100 mu .

ABEQ EP 616523 B UPAB: 19980330
Formulation comprises a particulate medicament (I) e.g. salmeterol, salbutamol, fluticasone propionate, becolomethasone **dipropionate** and a fluorocarbon or hydrogen-contg chlorofluorocarbon propellant.

Also claimed are the prepn of the **surface-modified** medicament and a canister for delivering metered doses of the **aerosol** formulation.

Pref., (I) is salmeterol xinafoate (Ia); salbutamol sulphate; fluticascone propionate; **beclomethasone dipropionate**; or a combination of salmeterol xinafoate and fluticasone propionate; or salbutamol and **beclomethasone dipropionate**. The propellant is pref. 1,1,1,2-tetrafluoroethane (II). (I) is present in an amt. of 0.005-10% wt. based on the total wt. of the formulation e.g. a salbutamol salt and 1,1,1,2-tetrafluoroethane in a ratio of 0.05:18 by wt. **Surface-modified** (I) are prepd. by admixture of particulate (I) with a non-polar, non-solvent liq. followed by removal of the lid.

USE/ADVANTAGE - The **aerosol** formulations are 'ozone friendly' using H-contg. chlorofluorocarbons as propellants and having no requirement for added **surfactants** or solvents for stabilising the constituent medicament(s). (I) can be used separately or in combination and may be e.g. analgesics, antiallergics, anti-infectives, antihistamines, anti-inflammatories, bronchodilators, diueretics, hormones, or therapeutic proteins and peptides. Admin. is by inhalation. Dosage of (I) is 50-2000 **micro**-g per day.
Dwg.0/0

L151 ANSWER 19 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1993-036124 [04] WPIX
DNC C1993-016343
TI Drug carrier system providing controlled and sustained release - comprises very small spherical particles esp. of albumin and opt. contg. bio adhesive polymer.
DC A96 B07
IN KREUTER, J; ZERBE, H; ZIMMER, A
PA (MINN) 3M MEDICA GMBH; (MINN) MINNESOTA MINING & MFG CO
CYC 16
PI WO 9300076 A1 19930107 (199304)* EN 20p A61K009-51 <--
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: JP US
DE 4120760 A1 19930304 (199310) 8p A61K009-14 <--
EP 591284 A1 19940413 (199415) EN A61K009-51 <--
R: DE FR GB IT
JP 06508369 W 19940922 (199442) A61K009-16 <--
ADT WO 9300076 A1 WO 1992-EP1425 19920624; DE 4120760 A1 DE 1991-4120760 19910624; EP 591284 A1 EP 1992-912498 19920624, WO 1992-EP1425 19920624; JP 06508369 W WO 1992-EP1425 19920624, JP 1993-501330 19920624
FDT EP 591284 A1 Based on WO 9300076; JP 06508369 W Based on WO 9300076
PRAI **DE 1991-4120760 19910624**
REP EP 486959; GB 1516348; WO 9004963
IC ICM **A61K009-14; A61K009-51**
ICS **A61K009-16**
AB WO 9300076 A UPAB: 19931119
Carrier system for drugs comprises (a) spherical particles of dia. below 1

micron or (b) spherical particles of dia. 1 nm-1 mm. plus a bioadhesive polymer (I).

In (a) the '**nanoparticles**' have dia. 100-300 nm. (I) has viscosity 4-100 mPa.s and is a neutral or anionic polymer while the particles are made of a (semi)synthetic or natural biopolymer, specifically albumin.

(I) is a polysaccharide, polyacrylate, alginate, polyvinyl alcohol, polyethylene glycol, polyvinylpyrrolidone or lectin, e.g. Na carboxymethylcellulose, hyaluronic acid or mucin. The carrier contains a drug (II) at (II):carrier wt. ratio 100:1-1:100 (esp. 2:1-1:2).

USE/ADVANTAGE - The carriers remain at the site of application for a long time and can be loaded with both hydrophilic and hydrophobic drugs to a high concn. to provide a stable drug concn. at the target site. The **nanoparticles** do not sediment in liq. (so can be formulated without **surfactant**) have a large specific surface area and can be used as carriers in inhalation **aerosols**. They are nontoxic, biodegradable, biocompatible, physically and chemically stable, non-antigenic, provide a controlled release of drug and are rapidly excreted. Carriers which include (I) show increased drug incorporation and a smaller dose is required. A particular application is treatment of eye diseases, e.g. glaucoma, inflammation, infection or allergies

Dwg.0/4

FS CPI
FA AB; DCN
MC CPI: A12-V01; A12-W05; B04-B04A6; B04-C02A2; B04-C02D; B04-C02E; B07-A02; B07-D09; B12-A01; B12-D02; B12-D07; B12-L04; B12-M10; B12-M11D

L151 ANSWER 20 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1992-199915 [24] WPIX
DNC C1992-090950
TI **Aerosol** drug formulations - contg. specified **surfactant** -coated drug particles in hydrogen-contg. fluorohydrocarbon or chloro-fluorohydrocarbon propellant.
DC B05 B07
IN BURNELL, P K P; TAYLOR, A J
PA (GLAX) GLAXO GROUP LTD
CYC 49
PI WO 9208447 A1 19920529 (199224)* EN 14p A61K009-12 <--
RW: AT BE BF BJ CF CG CH CI CM DE DK ES FR GA GB GN GR IT LU ML MR NL SE SN TD TG
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MC MG MN MW NL NO PL RO SD SE SU US
AU 9188629 A 19920611 (199237) A61K009-12 <--
EP 556239 A1 19930825 (199334) EN A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL
JP 06501693 W 19940224 (199413) 7p A61K031-44 <--
AU 653369 B 19940929 (199440) A61K009-12 <--
EP 556239 B1 19950830 (199539) EN 7p A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69112635 E 19951005 (199545) A61K009-12 <--
ES 2078550 T3 19951216 (199606) A61K009-12 <--
US 5785952 A 19980728 (199837) A61K009-12 <--
CA 2094727 C 20020115 (200215) EN A61K009-72 <--
ADT WO 9208447 A1 WO 1991-GB1961 19911107; AU 9188629 A AU 1991-88629 19911107, WO 1991-GB1961 19911107; EP 556239 A1 EP 1991-919478 19911107, WO 1991-GB1961 19911107; JP 06501693 W JP 1991-517432 19911107, WO 1991-GB1961 19911107; AU 653369 B AU 1991-88629 19911107; EP 556239 B1 EP 1991-919478 19911107, WO 1991-GB1961 19911107; DE 69112635 E DE 1991-612635 19911107, EP 1991-919478 19911107, WO 1991-GB1961 19911107; ES 2078550 T3 EP 1991-919478 19911107; US 5785952 A Cont of WO 1991-GB1961 19911107, Cont of US 1993-39425 19930429, Cont of US 1994-305816 19940914, US 1995-440441 19950512; CA 2094727 C CA 1991-2094727 19911107, WO 1991-GB1961 19911107

FDT AU 9188629 A Based on WO 9208447; EP 556239 A1 Based on WO 9208447; JP 06501693 W Based on WO 9208447; AU 653369 B Previous Publ. AU 9188629, Based on WO 9208447; EP 556239 B1 Based on WO 9208447; DE 69112635 E Based on EP 556239, Based on WO 9208447; ES 2078550 T3 Based on EP 556239; CA 2094727 C Based on WO 9208447
PRAI **GB 1990-24366 19901109**
REP EP 372777; WO 9111173; WO 9111495
IC ICM **A61K009-12**; **A61K009-72**; A61K031-44
ICS **A61K009-50**; A61K031-135; A61K031-56; A61K031-565; A61K047-06
AB WO 9208447 A UPAB: 19931025
Aerosol compsns. comprise **surfactant**-coated drug particles in a fluorohydrocarbon or chlorofluorohydrocarbon propellant. The drug is selected from salmeterol, fluticasone esters, 4-amino-3,5-dichloro-alpha (6-(2-(2-pyridyl)ethoxy)hexylaminomethyl) benzenemethanol (I) and their salts and solvents.
The propellant is pref. CF3CH2F. (I) is in R-enantiomer form. Salmeterol is used as its 1-hydroxy-2-naphthoate salt (II). The fluticasone ester is the propionate (III). The drug has a particle size of less than 100 **microns**, and is coated with 0.01-10 wt.% of benzalkonium chloride, lecithin, oleic acid or sorbitan trioleate.
ADVANTAGE - The compsns. has good stability without the need for cosolvents (cf. EP372777).
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B01-B03; B07-D04; B10-B03B; B10-H02B; **B12-M01A**
ABEQ EP 556239 A UPAB: 19931119
Aerosol compsns. comprise **surfactant**-coated drug particles in a fluorohydrocarbon or chlorofluorohydrocarbon propellant. The drug is selected from salmeterol, fluticasone esters, 4-amino-3,5-dichloro-alpha (6-(2-(2-pyridyl)ethoxy)hexylaminomethyl) benzenemethanol (I) and their salts and solvents.
The propellant is pref. CF3CH2F. (I) is in R-enantiomer form. Salmeterol is used as its 1-hydroxy-2-naphthoate salt (II). The fluticasone ester is the propionate (III). The drug has a particle size of less than 100 **microns**, and is coated with 0.01-10 wt.% of benzalkonium chloride, lecithin, oleic acid or sorbitan trioleate.
ADVANTAGE - The compsns. has good stability without the need for cosolvents (cf. EP372777).
ABEQ EP 556239 B UPAB: 19951004
An **aerosol** formulation comprising: (A) a medicament selected from th group comprising salmeterol, fluticasone esters, 4-amino-3,5-dichloro-alpha-(((6-(2-(2-pyridinyl)-ethoxy)hexyl)amino)methyl) benzene-methanol and physiologically acceptable salts and solvates thereof in particulate form and having a surface coating of a **surfactant**; and (B) a hydrogen-containing fluorocarbon or chlorofluorocarbon propellant.
Dwg.0/0

L151 ANSWER 21 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1992-199914 [24] WPIX
DNC C1992-090949
TI **Aerosol** drug formulations - contg. **surfactant**-coated drug particles, halo-hydrocarbon propellant and co solvent.
DC B05 B07
IN BURNELL, P K P; TAYLOR, A J
PA (GLAX) GLAXO GROUP LTD
CYC 49
PI WO 9208446 A1 19920529 (199224)* EN 8p A61K009-12 <--
RW: AT BE BF BJ CF CG CH CI CM DE DK ES FR GA GB GN GR IT LU ML MR NL SE SN TD TG
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MC MG MN

MW NL NO PL RO SD SE SU US

AU 9188778	A	19920611 (199237)			A61K009-12	<--
EP 556256	A1	19930825 (199334)	EN		A61K009-12	<--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL						
JP 06501700	W	19940224 (199413)		6p	A61K009-12	<--
AU 660952	B	19950713 (199535)			A61K009-12	<--
EP 556256	B1	19950830 (199539)	EN	6p	A61K009-12	<--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
DE 69112637	E	19951005 (199545)			A61K009-12	<--
ES 2078551	T3	19951216 (199606)			A61K009-12	<--
US 5919435	A	19990706 (199933)			A61K009-12	<--
JP 3210012	B2	20010917 (200156)		4p	A61K009-12	<--
US 6306368	B1	20011023 (200165)			A61K009-12	<--
CA 2094726	C	20020115 (200215)	EN		A61K009-72	<--

ADT WO 9208446 A1 WO 1991-GB1960 19911107; AU 9188778 A AU 1991-88778 19911107, WO 1991-GB1960 19911107; EP 556256 A1 EP 1991-919751 19911107, WO 1991-GB1960 19911107; JP 06501700 W JP 1991-518190 19911107, WO 1991-GB1960 19911107; AU 660952 B AU 1991-88778 19911107; EP 556256 B1 EP 1991-919751 19911107, WO 1991-GB1960 19911107; DE 69112637 E DE 1991-612637 19911107, EP 1991-919751 19911107, WO 1991-GB1960 19911107; ES 2078551 T3 EP 1991-919751 19911107; US 5919435 A Cont of WO 1991-GB1960 19911107, Cont of US 1993-39424 19930429, Cont of US 1994-305851 19940914, US 1995-440442 19950512; JP 3210012 B2 JP 1991-518190 19911107, WO 1991-GB1960 19911107; US 6306368 B1 Cont of WO 1991-GB1960 19911107, Cont of US 1993-39424 19930429, Cont of US 1994-305851 19940914, Cont of US 1995-440442 19950512, US 1998-198463 19981124; CA 2094726 C CA 1991-2094726 19911107, WO 1991-GB1960 19911107

FDT AU 9188778 A Based on WO 9208446; EP 556256 A1 Based on WO 9208446; JP 06501700 W Based on WO 9208446; AU 660952 B Previous Publ. AU 9188778, Based on WO 9208446; EP 556256 B1 Based on WO 9208446; DE 69112637 E Based on EP 556256, Based on WO 9208446; ES 2078551 T3 Based on EP 556256; JP 3210012 B2 Previous Publ. JP 06501700, Based on WO 9208446; US 6306368 B1 Cont of US 5919435; CA 2094726 C Based on WO 9208446

PRAI **GB 1990-24365 19901109**

REP EP 372777; US 4352789; WO 9104011

IC ICM **A61K009-12; A61K009-72**
ICS **A61K009-50**; A61K031-135; A61K031-137; A61K031-138; A61K031-56; A61K031-57; A61K047-06

AB WO 9208446 A UPAB: 20011206

Aerosol compsns. comprise **surfactant**-coated drug particles, a fluorohydrocarbon or chlorofluorohydrocarbon propellant, and a cosolvent that is more polar than the propellant. The wt. ratio of cosolvent to propellant is up to 5:100.

The drug is pref. salbutamol sulphate, salmeterol hydroxynaphthoate (I), **beclomethasone dipropionate** or fluticasone propionate. The propellant is CF3CH2F. The cosolvent is an aliphatic alcohol or polyol.

The drug has a particle size of less than 100 **microns** and is coated with 0.01-10wt.% of benzalkonium chloride, lecithin, oleic acid or sorbitan trioleate.

USE/ADVANTAGE - The compsns. are esp. useful for admin. of bronchodilators or antiinflammatory steroids by inhalation in the treatment of asthma. The compsns. have good stability. (cf. EP-372777) Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-B03; B10-A09A; B10-B03B; B10-E04C; B10-E04D; B12-D07; B12-K02; **B12-M01A; B12-M01B**

ABEQ EP 556256 A UPAB: 19931119

Aerosol compsns. comprise **surfactant**-coated drug particles, a fluorohydrocarbon or chlorofluorohydrocarbon propellant, and a cosolvent that is more polar than the propellant. The wt. ratio of cosolvent to propellant is up to 5:100.

The drug is pref. salbutamol sulphate, salmeterol hydroxynaphthoate (I), **beclomethasone dipropionate** or fluticasone propionate. The propellant is CF3CH2F. The cosolvent is an aliphatic alcohol or polyol.

The drug has a particle size of less than 100 **microns** and is coated with 0.01-10wt.% of benzalkonium chloride, lecithin, oleic acid or sorbitan trioleate.

USE/ADVANTAGE - The compsns. are esp. useful for admin. of bronchodilators or antiinflammatory steroids by inhalation in the treatment of asthma. The compsns. have good stability. (cf. EP-372777)

ABEQ EP 556256 B UPAB: 19951004
An **aerosol** formulation comprising: (A) a hydrogen-containing fluorocarbon or chlorofluorocarbon propellant; (B) a cosolvent having higher polarity than said propellant, which cosolvent is present in an amount of up to 5% w/w based upon propellant; and (C) a medicament in particulate form said medicament having a particle size of less than 100 **microm** and having a surface coating of a **surfactant**, which **surfactant** has no affinity for said propellant.
Dwg.0/0

L151 ANSWER 22 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1992-041362 [05] WPIX
DNN N1992-031821 DNC C1992-018107
TI **Aerosol** drug inhalation formulation - contains 1,1,1,2-tetra fluoroethane propellant and soluble **surfactant**.
DC B07 P34
IN JOHNSON, K A
PA (GLAX) GLAXO INC; (GLAX) GLAXO WELLCOME INC
CYC 39

PI	WO 9200107	A	19920109 (199205)*			A61L009-04	<--
	RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE						
	W: AT AU BB BG BR CA CH DE DK ES FI GB HU JP KP KR LK LU MC MG MW NL NO RO SD SE SU US						
	AU 9182135	A	19920227 (199218)				<--
	ZA 9104957	A	19920429 (199222)		16p	A61L	<--
	US 5126123	A	19920630 (199229)		5p	A61L009-04	<--
	EP 536250	A1	19930414 (199315)	EN	17p	A61L009-04	<--
	R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
	GB 2263064	A	19930714 (199328)		17p	A61L009-04	<--
	NZ 238749	A	19930727 (199333)			A61K009-12	<--
	PT 98105	A	19930831 (199338)			A61K009-12	<--
	JP 05507935	W	19931111 (199350)		8p	A61K009-12	<--
	AU 649702	B	19940602 (199427)			A61K009-12	<--
	GB 2263064	B	19940914 (199434)			A61L009-04	<--
	EP 536250	A4	19930616 (199526)			A61L009-04	<--
	PH 27744	A	19931103 (199823)			A61L009-04	<--
	RU 2098082	C1	19971210 (199831)		8p	A61K009-12	<--
	JP 3056784	B2	20000626 (200035)		8p	A61K009-12	<--
	KR 175164	B1	19990201 (200039)			A61K009-12	<--
	EP 536250	B1	20000906 (200044)	EN		A61K009-00	
	R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
	DE 69132407	E	20001012 (200059)			A61K009-00	
	ES 2151476	T3	20010101 (200107)			A61K009-00	

ADT ZA 9104957 A ZA 1991-4957 19910627; US 5126123 A CIP of US 1990-545437 19900628, US 1991-649405 19910201; EP 536250 A1 EP 1991-912299 19910627, WO 1991-US4715 19910627; GB 2263064 A WO 1991-US4715 19910627, GB 1992-23891 19921113; NZ 238749 A NZ 1991-238749 19910627; PT 98105 A PT 1991-98105 19910627; JP 05507935 W JP 1991-511820 19910627, WO 1991-US4715 19910627; AU 649702 B AU 1991-82135 19910627; GB 2263064 B WO 1991-US4715 19910627, GB 1992-23891 19921113; EP 536250 A4 EP 1991-912299 ; PH 27744 A PH 1991-42700 19910627; RU 2098082 C1 WO 1991-US4715 19910627, RU 1992-16609 19921225; JP 3056784 B2 JP 1991-511820 19910627, WO 1991-US4715 19910627; KR 175164 B1 WO 1991-US4715 19910627, KR 1992-703358 19921226;

EP 536250 B1 EP 1991-912299 19910627, WO 1991-US4715 19910627; DE 69132407 E DE 1991-632407 19910627, EP 1991-912299 19910627, WO 1991-US4715 19910627; ES 2151476 T3 EP 1991-912299 19910627

FDT EP 536250 A1 Based on WO 9200107; GB 2263064 A Based on WO 9200107; JP 05507935 W Based on WO 9200107; AU 649702 B Previous Publ. AU 9182135, Based on WO 9200107; GB 2263064 B Based on WO 9200107; JP 3056784 B2 Previous Publ. JP 05507935, Based on WO 9200107; EP 536250 B1 Based on WO 9200107; DE 69132407 E Based on EP 536250, Based on WO 9200107; ES 2151476 T3 Based on EP 536250

PRAI **US 1991-649405 19910201; US 1990-545437 19900628**

REP 1.Jnl.Ref; EP 372777; US 4352789; WO 9114422

IC ICM A61K009-00; **A61K009-12**; A61L005-44; A61L009-04
ICS **A61K009-72**; A61K047-06; A61K047-12; A61K047-14; A61K047-20; C09K003-30

AB WO 9200107 A UPAB: 19951004

Aerosol inhalation drug formulation comprises a **micronised** (inhalation) drug, 1,1,1,2-tetrafluoroethane (P134a) and a **surfactant** soluble in 1,1,1,2-tetrafluoroethane.

USE/ADVANTAGE - P134-a is known to have physical properties comparable with P12, it is non-flammable and has low potential for interaction with a wide variety of prods. sold in **aerosol** form, but its other chemical and solvent properties are different from P12. It is more environmentally acceptable than CFC propellants. P134-a-soluble **surfactants**, esp. soluble perfluorinated **surfactants** improve the stability of **micronised** inhalation drug suspensions in P134a (where perfluorinated and perfluoro mean that for at least one alkyl gp. all the H atoms are replaced by F). Thus when a **micronised** drug of average particle size up to 4 **microns** and max. particle size less than 10 **microns** and a P134a soluble **surfactant** are placed in P134a in a pressurised container, there is less tendency for the drug particles to aggregate and separate from the suspension than prior art. @(17pp Dwg.No.0/0/0

FS CPI GMPI

FA AB; DCN

MC CPI: B01-B03; B04-A06; B06-A01; B06-B02; B06-D04; B06-E05; B07-D04C; B10-B03B; B10-C04E; B10-H02B; B12-D02; B12-E04; B12-G04; B12-K02; **B12-M01A**; **B12-M01B**; B12-M09

ABEQ US 5126123 A UPAB: 19931006

Aerosol inhalation drug formulation comprises a **micronised** inhalation drug and a 1,1,1,2-tetrafluoroethane-soluble, perfluoronated **surfactant** in suspension in 1,1,1,2-tetrafluoroethane.

Drug is pref. albuterol, salmeterol, amiloride, fluticasonepropionate, **beclomethasone dipropionate** of (-)-4-amino-3,5-dichlon- alpha-(((6-(2-pyridinyl) ethoxy)-hexyl)amino)methyl) benzenemethanol.

USE/ADVANTAGE - Useful for antiallergic, respiratory (e.g. antiasthmatic and bronchodilating), antibiotic, antiinflammatory, antifungal, analgesic, antiviral and cardiovascular drugs.

ABEQ GB 2263064 A UPAB: 19931116

Aerosol inhalation drug formulation comprises a **micronised** (inhalation) drug, 1,1,1,2-tetra:fluoroethane (P134a) and a **surfactant** soluble in 1,1,1,2-tetra:fluoroethane.

USE/ADVANTAGE - P134-a is known to have physical properties comparable with P12, it is non-flammable and has low potential for interaction with a wide variety of prods. sold in **aerosol** form, but its other chemical and solvent properties are different from P12. It is more environmentally acceptable than CFC propellants. P134-a-soluble **surfactants**, esp. soluble perfluorinated **surfactants** improve the stability of **micronised** inhalation drug suspensions in P134a (where perfluorinated and perfluoro mean that for at least one alkyl gp. all the H atoms are replaced by F). Thus when a

micronised drug of average particle size up to 4 **microns** and max. particle size less than 10 **microns** and a P134a soluble **surfactant** are placed in P134a in a pressurised container, there is less tendency for the drug particles to aggregate and separate from the suspension than prior art.
Dwg.0/0

ABEQ GB 2263064 B UPAB: 19941013
An **aerosol** inhalation drug formulation comprising a particulate inhalation drug having a maximum particle size of less than 10 **microns**, 1,1,1,2-tetrafluoroethane as propellant, and a perfluorinated **surfactant** soluble in 1,1,1,2-tetrafluoroethane, which formulation is substantially free of an adjuvant having a higher polarity than 1,1,1,2-tetrafluoroethane, with the proviso that said **surfactant** is other than perfluorobutanoic acid, perfluorooctanoic acid or a perfluorinated sulfonamido alcohol phosphate ester.

L151 ANSWER 23 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1992-041324 [05] WPIX
DNC C1992-018069
TI **Aerosol** medicament compsns. - contg. fluoro-hydrocarbon propellant and ethoxylated **surfactant**.
DC A96 B07
IN BOOLES, C; SOMANI, A
PA (FISO) FISONS PLC
CYC 41
PI WO 9200061 A 19920109 (199205)* A61K009-12 <--
RW: AT BE CH DE DK ES FR GB IT LU NL OA SE
W: AU BB BG BR CA CS FI HU JP KP KR LK MC MW NO PL RO SD SU US
AU 9180556 A 19920227 (199218) <--
ZA 9104897 A 19920325 (199218) 13p <--
PT 98133 A 19920430 (199222) A61K009-00 <--
NZ 238746 A 19921028 (199301) A61K009-12 <--
FI 9205852 A 19921223 (199312) A61K000-00 <--
EP 536235 A1 19930414 (199315) EN 12p A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
NO 9204954 A 19921221 (199316) A61K009-12 <--
BR 9106595 A 19930420 (199320) A61K009-12 <--
CZ 9203925 A3 19930512 (199335) A61K009-12 <--
HU 63554 T 19930928 (199344) A61K009-12 <--
JP 05507712 W 19931104 (199349) 7p A61K009-12 <--
IL 98666 A 19940412 (199422) C09K003-30 <--
SK 9203925 A3 19940706 (199432) A61K009-12 <--
EP 536235 B1 19970122 (199709) EN 10p A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69124374 E 19970306 (199715) A61K009-12 <--
ES 2096653 T3 19970316 (199718) A61K009-12 <--
US 5846521 A 19981208 (199905) A61K009-12 <--
JP 2854974 B2 19990210 (199911) 5p A61K009-12 <--
CA 2085884 C 20011204 (200203) EN A61K009-12 <--
ADT ZA 9104897 A ZA 1991-4897 19910625; PT 98133 A PT 1991-98133 19910628; NZ 238746 A NZ 1991-238746 19910627; FI 9205852 A WO 1991-GB1023 19910625, FI 1992-5852 19921223; EP 536235 A1 EP 1991-912173 19910625, WO 1991-GB1023 19910625; NO 9204954 A WO 1991-GB1023 19910625, NO 1992-4954 19921221; BR 9106595 A BR 1991-6595 19910625, WO 1991-GB1023 19910625; CZ 9203925 A3 CS 1992-3925 19921228; HU 63554 T WO 1991-GB1023 19910625, HU 1992-4098 19910625; JP 05507712 W JP 1991-511396 19910625, WO 1991-GB1023 19910625; IL 98666 A IL 1991-98666 19910628; SK 9203925 A3 CS 1992-3925 19921228, WO 1991-GB1023 ; EP 536235 B1 EP 1991-912173 19910625, WO 1991-GB1023 19910625; DE 69124374 E DE 1991-624374 19910625, EP 1991-912173 19910625, WO 1991-GB1023 19910625; ES 2096653 T3 EP 1991-912173 19910625; US 5846521 A Cont of WO 1991-GB1023 19910625, Cont of US 1991-965382 19921214, Cont of US 1994-280301 19940726, Cont of US 1995-449997 19950525, US 1997-892169 19970714; JP 2854974 B2 JP 1991-511396 19910625, WO

1991-GB1023 19910625; CA 2085884 C CA 1991-2085884 19910625, WO 1991-GB1023 19910625

FDT EP 536235 A1 Based on WO 9200061; BR 9106595 A Based on WO 9200061; HU 63554 T Based on WO 9200061; JP 05507712 W Based on WO 9200061; EP 536235 B1 Based on WO 9200061; DE 69124374 E Based on EP 536235, Based on WO 9200061; ES 2096653 T3 Based on EP 536235; JP 2854974 B2 Previous Publ. JP 05507712, Based on WO 9200061; CA 2085884 C Based on WO 9200061

PRAI **GB 1990-14526 19900629; GB 1990-14527 19900629 ; GB 1990-23953 19901103; WO 1991-GB1023 19910625**

REP EP 372777; GB 2046093; WO 8807855; WO 9011754

IC ICM A61K000-00; A61K009-00; **A61K009-12**; C09K003-30
ICS **A61K009-72**; A61K047-34

AB WO 9200061 A UPAB: 19931006
Pressurised **aerosol** compsns. comprise a medicament (I) a hydrofluorocarbon propellant (II) and a polyethoxylated **surfactant** (III).

The compsns. contain 0.01-10 (esp. 0.1-5) wt.% (III) and 0.1-10 (esp. 0.5-5) wt.% (I), where (I) has a particle size of 1-5 **microns**. (I) is a nedocromil or cromoglycate salt. (II) is CF3CHFCF3. (III) is an ethylene oxide/propylene oxide copolymer or an ethoxylated alkylphenol, alcohol, diamine or polyol, esp. a polyoxyethylene sorbitan monooleate.

USE/ADVANTAGE - The compsns. are esp. useful for admin. of powdered medicaments by inhalation. No organic solvent is required to maintain the **surfactant** in soln. (cf. EP-372777).

0/0

FS CPI

FA AB; DCN

MC CPI: A12-V01; A12-W12C; B04-C03C; B06-A01; B06-E05; B10-H02B; **B12-M01A**

ABEQ JP 05507712 W UPAB: 19940126
Pressurised **aerosol** compsns. comprise a medicament (I), a hydrofluorocarbon propellant (II) and a polyethoxylated **surfactant** (III).

The compsns. contain 0.01-10 (esp. 0.1-5) wt.% (III) and 0.1-10 (esp. 0.5-5) wt.% (I), where (I) has a particle size of 1-5 **microns**. (I) is a nedocromil or cromoglycate salt. (II) is CF3CHFCF3. (III) is an ethylene oxide/propylene oxide copolymer or an ethoxylated alkylphenol, alcohol, diamine or polyol, esp. a polyoxyethylene sorbitan monooleate.

USE/ADVANTAGE - The compsns. are esp. useful for admin. of powdered medicaments by inhalation. No organic solvent is required to maintain the **surfactant** in soln..

Dwg.0/0

ABEQ EP 536235 B UPAB: 19970228
A pressurised **aerosol** composition comprising a medicament, a hydrofluorocarbon propellant and a polyethoxylated **surfactant**, characterised in that the composition contains no solvent, other than the propellant, capable of increasing the solubility of the **surfactant** in the propellant.

Dwg.0/0

L151 ANSWER 24 OF 38 WPIX (C) 2002 THOMSON DERWENT

AN 1991-339531 [46] WPIX

DNC C1991-146530

TI Pharmaceutical **aerosol** formulation - comprises biologically active polypeptide easy administered to respiratory tract.

DC A96 B04

IN NARUSE, N; PLATZ, R M; SATOH, Y; UTSUMI, J

PA (TORA) TORAY IND INC

CYC 16

PI WO 9116038 A 19911031 (199146)* <--
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: JP KR

EP 477386 A 19920401 (199214) 30p <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 05000963 A 19930108 (199306) 5p A61K037-02 <--
JP 05500229 W 19930121 (199308) 10p A61K037-02 <--
EP 477386 B1 19970723 (199734) EN 12p A61K009-12 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69126935 E 19970828 (199740) A61K009-12 <--

ADT EP 477386 A EP 1991-907509 19910412; JP 05000963 A JP 1990-98353 19900413; JP 05500229 W JP 1991-507025 19910412, WO 1991-JP486 19910412; EP 477386 B1 EP 1991-907509 19910412, WO 1991-JP486 19910412; DE 69126935 E DE 1991-626935 19910412, EP 1991-907509 19910412, WO 1991-JP486 19910412

FDT JP 05500229 W Based on WO 9116038; EP 477386 B1 Based on WO 9116038; DE 69126935 E Based on EP 477386, Based on WO 9116038

PRAI **JP 1990-98353 19900413**

REP EP 122036; EP 257956; EP 289336; EP 396903; WO 8905158; EP 215658

IC ICM **A61K009-12**; A61K037-02
ICS **A61K009-14**; **A61K009-51**; **A61K009-72**; A61K037-04; A61K037-66; A61K038-21; A61K045-02; A61K047-26; A61K047-42

AB WO 9116038 A UPAB: 19930928
Pharmaceutical **aerosol** formulation comprises (a) solid **micronised** particles of a biologically active polypeptide selected from human interferon and human interleukin, the median size of particles being 0.5-10mm; and opt. (b) (i) human serum albumin, sugar or sugar alcohol; and (ii) a **surfactant**.

The solid **micronised** particles pref. additionally contains human serum albumin, sugar or sugar alcohol. The formulation includes a **surfactant** selected from sorbitan trioleate, soya lecithin, oleyl alcohol and/or polyoxyethylene hydrogenated castor oil. The active polypeptide is human interferon pref. human interferon -B or human interleukin pref. human interleukin-6.

USE/ADVANTAGE - The biologically active polypeptide is administered easily to the respiratory tract and does not lsoe its activity by oxidn., aggregation or autolysis. Since it is solid not in aq. soln. @(30pp Dwg.No.0/3)

FS CPI

FA AB; DCN

MC CPI: A12-V01; B02-V03; B04-B01B; B04-B01C; B04-B04D2; B04-C01G; B04-D01; B07-A02; B10-A07; **B12-M01A**; B12-M07

ABEQ EP 477386 A UPAB: 19930928
Pharmaceutical **aerosol** formulation comprises (a) solid **micronised** particles of a biologically active polypeptide selected from human interferon and human interleukin, the media size of particles being 0.5-10mm; and (b) (i) human serum albumin, sugar or sugar alcohol; and (ii) a **surfactant**.

The solid **micronised** particles pref. additionally contains human serum albumin, sugar or sugar alcohol. The formulation includes a **surfactant** selected from sorbitan trioleate, soya lecithin, oleyl alcohol and/or polyoxyethylene hydrogenated castor oil. The active polypeptide is human interferon pref. human interferon-B or human interleukin, pref. human interleukin-6.

USE/ADVANTAGE - The biologically active polypeptide is administered easily to the respiratory tract and does not lose its activity by oxidn., aggregation or autolysis. Since it is solid not in aq. soln..

ABEQ JP 05500229 W UPAB: 19930928
Pharmaceutical **aerosol** formulation comprises (a) solid **micronised** particles of a biologically active polypeptide selected from human interferon and human interleukin, the median size of particles being 0.5-10mm; and opt. (b) (i) human serum albumin, sugar or sugar alcohol; and (ii) a **surfactant**.

The solid **micronised** particles pref. additionally contain human serum albumin, sugar or sugar alcohol. The formulation includes a **surfactant** selected from sorbitan trioleate, soya lecithin, oleyl

alcohol and/or polyoxyethylene hydrogenated castor oil. The active polypeptide is human interferon pref. human interferon-B or human interleukin, pref. human interleukin-6.

USE/ADVANTAGE - The biologically active polypeptide is administered easily to the respiratory tract and does not lose its activity by oxidn., aggregation or autolysis, since it is solid and not in an aq. soln.

ABEQ EP 477386 B UPAB: 19970820

A pharmaceutical **aerosol** formulation comprising solid **micronised** particles of a biologically active human interferon beta, human serum albumin and a sugar or a sugar alcohol, wherein the median size of the particles is in the range of 0.5 to 10 **micro** m.

Dwg.0/3

L151 ANSWER 25 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1991-225090 [31] WPIX
DNC C1991-097694
TI Atropine and salbutamol compsn. for **aerosol** inhaler - gives enhanced, longer lasting bronchodilation.
DC B02 B05
IN LESLIE, S T; MALKOWSKA, S T A; MILLER, R B; MALKOWSKA, A; THERESE, S
PA (EURO-N) EUROCELTIQUE SA
CYC 19
PI GB 2240271 A 19910731 (199131)* <--
NO 9100186 A 19910718 (199138) <--
CA 2034246 A 19910718 (199139) <--
AU 9169321 A 19910718 (199141) <--
FI 9100237 A 19910718 (199141) <--
EP 496138 A1 19920729 (199231) EN 8p A61K031-46 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 04210918 A 19920803 (199237) 5p A61K031-46 <--
ADT GB 2240271 A GB 1991-100488 19910110; EP 496138 A1 EP 1991-300195 19910111; JP 04210918 A JP 1991-14712 19910114
PRAI **GB 1990-1019 19900117**
REP 04Jnl.Ref; WO 8606959
IC ICM A61K031-46
ICS **A61K009-12**; **A61K009-72**; A61K031-13; A61K031-135
ICA C07C215-60
ICI A61K031-46, A61K031:135
AB GB 2240271 A UPAB: 19930928

A pressurised, metered-dose **aerosol** contains an orally inhalable, pharmaceutical compsn. comprising; (a) salbutamol sulphate, at least 90% by wt. of which has a particle size less than 10 **microns** ; (b) atropine methonitrate, particle size as for the salbutamol sulphate; (c) at least one of a **surfactant** and a wetting agent; and (d) an **aerosol** propellant for suspension of the above. Each actuation of the **aerosol** valve delivers salbutamol sulphate, equiv. to 50 - 200 mcg salbutamol and atropine methonitrate equiv. to 50 - 300 mcg atropine.

USE/ADVANTAGE - The compsn. gives enhanced and longer lasting bronchodilation than salbutamol alone. It is used in treatment of asthma.

0/0

FS CPI
FA AB; DCN
MC CPI: B06-D04; B10-B03B; B12-D02; B12-K02; B12-M11

L151 ANSWER 26 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1990-290140 [38] WPIX
DNC C1990-125236
TI Self-propelled therapeutic **aerosol** suspension for inhalation - contg. **micronised** drug-extender complex, solvent and/or **surfactant** and propellant mixt..
DC B04 B07

IN FELT, G R; WARCHOL, M P
PA (RORE) RORER INT OVERSEAS INC
CYC 19
PI WO 9009781 A 19900907 (199038)* <--
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: AU BR CA FI JP NO
AU 9051949 A 19900926 (199050) <--
FI 9103899 A 19910819 (199147) <--
EP 460064 A 19911211 (199150) <--
R: AT BE CH DE ES FR GB IT LI LU NL SE
NO 9103298 A 19911022 (199205) <--
JP 05508616 W 19931202 (199402) 13p A61K009-12 <--
EP 460064 A4 19920401 (199521) <--
ADT EP 460064 A EP 1990-904101 19900221; JP 05508616 W JP 1990-504385 19900221, WO 1990-US928 19900221; EP 460064 A4 EP 1990-904101
FDT JP 05508616 W Based on WO 9009781
PRAI **US 1989-314605 19890223**
REP US 4241051; US 4690952; US 4758550; US 4788221; US 4895719; 2.Jnl.Ref; EP 302772; GB 837465; GB 994734; JP 60161924
IC **A61K009-12**; A61K037-02; C07K007-36
ICM **A61K009-12**
ICS **A61K009-72**; A61K037-02; C07K007-36
AB WO 9009781 A UPAB: 19930928
A self-propelled therapeutic **aerosol** suspension for inhalation is claimed comprising (a) 0.01-5 wt% of a water soluble, propellant insoluble solid homogeneous complex in **micronised** form of at least one active drug and an extender, the active drug comprising 0.1-25 wt% of the drug/extender complex. (b) 0.1-3 wt% of a solvent (eg EtOH) and/or **surfactant** (eg oleic acid) and (c) 92-99.89 wt% of a propellant mixt.

The propellant mixt is pref 90 wt% CCl2F2 and 10 wt% dichlorotetrafluoroethane or 10 wt% CCl3F. The extender is pref DL-methionine.

USE/ADVANTAGE - The inhalation therapy provides rapid medication effects and a redn of systemic side effects. The active drug may be a polypeptide, esp a calcitonin or analogue for the treatment of diseases characterised by hypercalcemia and high phosphate concns in the blood, eg hyperpara thyroidism, idiopathic hypercalcemia of infancy, Paget's disease, vitamin D intoxication or osteolytic bone metastases.
0/0
FS CPI
FA AB; DCN
MC CPI: B04-B02D3; B04-C01; B10-B02D; B10-C04E; B10-E04D; B10-H02B; B12-G01; B12-G07; B12-H05; B12-J05; B12-J08; **B12-M01A**

L151 ANSWER 27 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1990-180559 [24] WPIX
CR 1992-278075 [34]; 1995-180525 [24]; 2000-294921 [26]
DNC C1990-078345
TI Pharmaceutical **aerosol** contg. tetra fluoroethane, **surfactant** and polar cpd. - free of chloro fluorocarbon(s), for delivering anti-asthma agents by oral or nasal inhalation.
DC A96 B07 P34
IN GREENLEAF, D J; PUREWAL, T S
PA (RIKL) RIKER LAB INC
CYC 19
PI EP 372777 A 19900613 (199024)* 10p <--
R: BE CH DE ES FR GB IT LI NL SE
AU 8945956 A 19900614 (199034) <--
CA 2004598 A 19900606 (199034) <--
DK 8905957 A 19900607 (199034) <--
JP 02200627 A 19900808 (199038) <--
ZA 8909290 A 19910626 (199131) <--

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     EP 372777     B1 19930107 (199302)  EN   14p    A61K009-12      <--
         R: BE CH DE ES FR GB IT LI NL SE
     DE 68904300   E  19930218 (199308)             A61K009-12      <--
     US 5225183    A  19930706 (199328)        6p   A61L009-04      <--
     NZ 231579     A  19931125 (199350)             A61K009-12      <--
     NZ 243056     A  19931125 (199350)             A61K009-12      <--
     ES 2045470    T3 19940116 (199407)             A61K009-12      <--
     IL 92457      A  19941021 (199443)             A61K009-12      <--
     US 5439670    A  19950808 (199537)#       8p   A61L009-04      <--
     US 5605674    A  19970225 (199714)        7p   A61L009-04
     US 5674473    A  19971007 (199746)        7p   A61L009-04
     US 5681545    A  19971028 (199749)#       7p   A61L009-04
     US 5683677    A  19971104 (199750)        7p   A61L009-04
     US 5695743    A  19971209 (199804)        5p   A61L009-04
     US 5720940    A  19980224 (199815)        8p   A61L009-04
     US 5766573    A  19980616 (199831)             A61L009-04
     US 5776434    A  19980707 (199834)             A61L009-04
     JP 2786493    B2 19980813 (199837)        8p   A61K009-12      <--
     KR 154116     B1 19981116 (200029)             A61K009-12      <--
     CA 2303601    A1 19900606 (200041)  EN         A61K009-12      <--
     CA 2004598    C  20001107 (200061)  EN         A61K009-12      <--
ADT  EP 372777 A EP 1989-312270 19891127; JP 02200627 A JP 1989-317415
     19891206; ZA 8909290 A ZA 1989-9290 19891205; EP 372777 B1 EP 1989-312270
     19891127; DE 68904300 E DE 1989-604300 19891127, EP 1989-312270 19891127;
     US 5225183 A Cont of US 1989-442119 19891128, US 1991-649140 19910130; NZ
     231579 A NZ 1989-231579 19891129; NZ 243056 A NZ 1989-243056 19891129; ES
     2045470 T3 EP 1989-312270 19891127; IL 92457 A IL 1989-92457 19891127; US
     5439670 A Cont of US 1989-442119 19891128, Cont of US 1991-649140
     19910130, US 1993-86820 19930702; US 5605674 A Cont of US 1989-442119
     19891128, Div ex US 1991-649140 19910130, Div ex US 1993-26476 19930304,
     US 1995-471618 19950531; US 5674473 A Cont of US 1989-442119 19891128, Div
     ex US 1991-649140 19910130, Div ex US 1993-26476 19930304, US 1995-455870
     19950531; US 5681545 A Cont of US 1989-442119 19891128, Div ex US
     1991-649140 19910130, Div ex US 1993-26476 19930304, US 1995-471616
     19950531; US 5683677 A Cont of US 1989-442119 19891128, Div ex US
     1991-649140 19910130, Cont of US 1993-26476 19930304, US 1995-455012
     19950531; US 5695743 A Cont of US 1989-442119 19891128, Div ex US
     1991-649140 19910130, US 1993-26476 19930304; US 5720940 A Cont of US
     1989-442119 19891128, Div ex US 1991-649140 19910130, Div ex US 1993-26476
     19930304, US 1995-792209 19950531; US 5766573 A Cont of US 1989-442119
     19891128, Div ex US 1991-649140 19910130, Div ex US 1993-26476 19930304,
     Cont of US 1995-455880 19950531, US 1997-783737 19970116; US 5776434 A
     Cont of US 1989-442119 19891128, Div ex US 1991-649140 19910130, Div ex US
     1993-26476 19930304, Cont of US 1995-455638 19950531, US 1997-784436
     19970116; JP 2786493 B2 JP 1989-317415 19891206; KR 154116 B1 KR
     1989-17929 19891205; CA 2303601 A1 Div ex CA 1989-2004598 19891205, CA
     1989-2303601 19891205; CA 2004598 C CA 1989-2004598 19891205
FDT  DE 68904300 E Based on EP 372777; NZ 243056 A Div ex NZ 231579; ES 2045470
     T3 Based on EP 372777; US 5439670 A Cont of US 5225183; US 5605674 A Div
     ex US 5225183; US 5674473 A Div ex US 5225183; US 5681545 A Div ex US
     5225183; US 5683677 A Div ex US 5225183; US 5695743 A Div ex US 5225183;
     US 5720940 A Div ex US 5225183; US 5766573 A Div ex US 5225183, Div ex US
     5695743; US 5776434 A Div ex US 5225183, Div ex US 5695743; JP 2786493 B2
     Previous Publ. JP 02200627
PRAI GB 1988-28477    19881206; US 1993-86820    19930702
     ; US 1995-471616   19950531
REP  1.Jnl.Ref; A3...199047; DE 2737132; GB 2046093; NoSR.Pub; US 4174295
IC   ICM  A61K009-12; A61L009-04
     ICS  A61K009-00; A61K009-72; A61K047-00; A61K047-06; A61M011-04;
          C09K003-30
AB   EP    372777 A UPAB: 20001128
       Aerosol formulation contains a pharmaceutical (I);
     1,1,1,2-tetrafluoroethane (II); a surfactant (III) and at least
```

one cpd. (IV) more polar than (II).

Specifically the formulation contains no CHClF2, CH2F2 or CF3CH3, and (IV) is e.g. an alcohol and/or satd. hydrocarbon, e.g. EtOH, isopropanol, n-; iso- or neo-pentane, and/or isopropyl myristate.

(I) is salbutamol, **beclomethasone, dipropionate,** disodium cromoglycate, pirbuterol, isoprenaline, adrenaline, rimiterol or ipratropium bromide, esp. at 0.01-5 wt.%.

USE/ADVANTAGE - The compsns. are used to deliver a wide range of drug, by oral or nasal inhalation, esp. for treatment of asthma. They can be made free of CFCs and the addn. of (IV) allows larger amts. of (III) to be dissolved, producing stable and homogeneous suspensions of (I) particles.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; A12-W12C; B01-B03; B04-C03C; B06-A01; B06-D04; B07-D04C; B07-D05; B10-B03B; B10-E04D; B10-G02; B10-H02B; B10-J02; B12-D02; B12-K02; **B12-M01A**; B12-M09

ABEQ EP 372777 B UPAB: 19930928

A medicinal **aerosol** formulation suitable for administration to a patient by oral or nasal inhalation comprising a medicament, 1,1,1,2-tetrafluoroethane, a **surface active** agent and at least one cpd. having a higher polarity than 1,1,1,2-tetrafluoroethane, the formulation being in the form of a soln. or a suspension of medicament particles having a median particle size of less than 10 **microns** and being substantially free of CHCIF2, CH2F2, and CF3CH3.

0/0

ABEQ US 5225183 A UPAB: 19931116

Aerosol formulation comprises: (a) a medicament; (b) a propellant free of chlorofluorocarbons, comprising 1,1,1,2-tetrafluoroethane (TFE); (c) a **surfactant** to stabilise the formulation or to lubricate a valve stem in a metering valve; and (d) at least one of EtOH, iPrOH, n-pentane, isopentane, neopentane, isopropyl and myristate (sic), in an amt.miscible with TFE, the **surfactant** being soluble in the formulation in a greater amt. than in TFE. The medicament is pref. salbutamol, **beclomethasone, dipropionate**, disodium-cromoglycate, pirbuterol, isoprenaline, adrenalin, rimiterol or ipratropium bromide.

USE/ADVANTAGE - For pulmonary, nasal, buccal or topical admin. is metered doses.

Dwg.0/0

ABEQ US 5439670 A UPAB: 19950921

Aerosol formulation comprises (a) a medicament; (b) a propellant; (c) a **surface active** agent; and (d) 1 or more other cpd. having higher polarity than 1,1,1,2-tetrafluoroethane w.r.t. Kauributanol value. Cpd. (b) comprises 1,1,1,2-tetrafluoroethane and less than 5% of CHClF2, CH2F2, and/or CF3CH3. Cpd. (d) is e.g. ethyl alcohol, isopropyl alcohol, propylene glycol, propane, etc.

USE/ADVANTAGE - For pulmonary, nasal, buccal or topical administration of medicine. Formulation is free of chlorofluorocarbons.

Dwg.0/0

ABEQ US 5605674 A UPAB: 19970407

An **aerosol** formulation contained in an **aerosol** container equipped with a metering valve, comprises: (a) a therapeutically effective amount of a medicament; and (b) a propellant free of chlorofluorocarbons, comprising 1,1,1,2-tetrafluoroethane.

The formulation is suitable for delivery to the lung by inhalation from the **aerosol** container.

Dwg.0/0

ABEQ US 5674473 A UPAB: 19971119

Preparation of solution **aerosol** formulation suitable for delivery to the lung by inhalation, comprises:

(a) providing an **aerosol** container;

(b) charging to the container:
(i) a medicament in an amount sufficient to provide a number of therapeutically effective doses of the formulation,
(ii) an amount of propellant sufficient to propel from the container the number of therapeutically effective doses, the propellant being free of chlorofluorocarbons and comprising 1,1,1,2-tetrafluoroethane; and
(c) solubilizing the medicament.
Dwg.0/0

ABEQ US 5681545 A UPAB: 19971211
A method of making a suspension **aerosol** formulation suitable for delivery to the lung by inhalation comprising the steps of:
(a) providing an **aerosol** container, and
(b) charging to said container:
(i) a medicament in an mount sufficient to provide a plurality of therapeutically effective doses,
(ii) an amount of propellant sufficient to propel from said container said plurality of therapeutically effective doses, said propellant being substantially free of chlorofluorocarbons and comprising 1,1,1,2-tetrafluoroethane; and
(c) dispersing said medicament.
Dwg.0/0

ABEQ US 5683677 A UPAB: 19971217
A medicinal **aerosol** formulation, comprising:
(a) a therapeutically effective amount of a medicament;
(b) a propellant substantially free of chlorofluorocarbons and comprising 1,1,1,2-tetrafluoroethane; and
(c) wherein the medicament is fully dissolved in the formulation, and said formulation is suitable for delivery by inhalation.
Dwg.0/0

ABEQ US 5695743 A UPAB: 19980126
Aerosol formulation contains a pharmaceutical (I); 1,1,1,2-tetrafluoroethane (II); a **surfactant** (III) and at least one cpd. (IV) more polar than (II).
Specifically the formulation contains no CHClF2, CH2F2 or CF3CH3, and (IV) is e.g. an alcohol and/or satd. hydrocarbon, e.g. EtOH, isopropanol, n-; iso- or neo-pentane, and/or isopropyl myristate.
(I) is salbutamol, **beclomethasone, dipropionate**, disodium cromoglycate, pirbuterol, isoprenaline, adrenaline, rimiterol or ipratropium bromide, esp. at 0.01-5 wt.%.
USE/ADVANTAGE - The compsns. are used to deliver a wide range of drug, by oral or nasal inhalation, esp. for treatment of asthma. They can be made free of CFCs and the addn. of (IV) allows larger amts. of (III) to be dissolved, producing stable and homogeneous suspensions of (I) particles.
Dwg.0/0

ABEQ US 5720940 A UPAB: 19980410
Aerosol formulation contains a pharmaceutical (I); 1,1,1,2-tetrafluoroethane (II); a **surfactant** (III) and at least one cpd. (IV) more polar than (II).
Specifically the formulation contains no CHClF2, CH2F2 or CF3CH3, and (IV) is e.g. an alcohol and/or satd. hydrocarbon, e.g. EtOH, isopropanol, n-; iso- or neo-pentane, and/or isopropyl myristate.
(I) is salbutamol, **beclomethasone, dipropionate**, disodium cromoglycate, pirbuterol, isoprenaline, adrenaline, rimiterol or ipratropium bromide, esp. at 0.01-5 wt.%.
USE/ADVANTAGE - The compsns. are used to deliver a wide range of drug, by oral or nasal inhalation, esp. for treatment of asthma. They can be made free of CFCs and the addn. of (IV) allows larger amts. of (III) to be dissolved, producing stable and homogeneous suspensions of (I) particles.
Dwg.0/0

L151 ANSWER 28 OF 38 WPIX (C) 2002 THOMSON DERWENT

AN 1988-353793 [49] WPIX
DNC C1988-156489
TI **Microsphere** drug delivery systems - contg. drug and **surfactant** to enhance trans-mucosal absorption.
DC B07
IN ILLUM, L
PA (COSM-N) COSMAS-DAMIAN LTD; (DANB-N) DANBIOSYST UK LTD
CYC 19
PI WO 8809163 A 19881201 (198849)* EN 42p <--
RW: AT BE CH DE FR GB IT LI LU NL SE
W: AU CH DK FI GR JP NO US
AU 8817931 A 19881221 (198916) <--
NO 8900283 A 19890328 (198918) <--
FI 8905555 A 19891121 (199010) <--
DK 8905837 A 19900118 (199016) <--
EP 391896 A 19901017 (199042) <--
R: AT BE CH DE FR GB IT LI LU NL SE
GB 2231495 A 19901121 (199047) <--
JP 02503915 W 19901115 (199101) <--
GB 2231495 B 19910828 (199135) <--
CA 1324079 C 19931109 (199351) A61K009-16 <--
EP 391896 B1 19940302 (199409) EN 22p A61K009-16 <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3888201 G 19940407 (199415) A61K009-16 <--
NO 178564 B 19960115 (199608) A61K009-16 <--
FI 97444 B 19960913 (199642) A61K009-16 <--
US 5690954 A 19971125 (199802) 29p A61K009-16 <--
US 5863554 A 19990126 (199911) A61K009-16 <--
JP 2914670 B2 19990705 (199932) 18p A61K009-107
ADT WO 8809163 A WO 1988-GB396 19880520; EP 391896 A EP 1988-904570 19880520; GB 2231495 A GB 1988-24696 19880520; CA 1324079 C CA 1988-567452 19880520; EP 391896 B1 EP 1988-904570 19880520, WO 1988-GB396 19880520; DE 3888201 G DE 1988-3888201 19880520, EP 1988-904570 19880520, WO 1988-GB396 19880520; NO 178564 B WO 1988-GB396 19880520, NO 1989-283 19890123; FI 97444 B WO 1988-GB396 19880520, FI 1989-5555 19891121; US 5690954 A Cont of WO 1988-GB396 19880520, Cont of US 1989-424320 19891120, CIP of US 1991-760854 19910917, Cont of US 1992-865855 19920409, Cont of US 1993-142844 19931025, US 1995-412094 19950328; US 5863554 A Cont of US 1989-424320 19891120, CIP of US 1991-760854 19910917, Cont of US 1992-865855 19920409, Cont of US 1993-142844 19931025, Div ex US 1995-412094 19950328, US 1997-899976 19970724; JP 2914670 B2 JP 1988-504488 19880520, WO 1988-GB396 19880520
FDT EP 391896 B1 Based on WO 8809163; DE 3888201 G Based on EP 391896, Based on WO 8809163; NO 178564 B Previous Publ. NO 8900283; FI 97444 B Previous Publ. FI 8905555; US 5863554 A Div ex US 5690954; JP 2914670 B2 Previous Publ. JP 02503915, Based on WO 8809163
PRAI **GB 1987-12176 19870522; GB 1988-24696 19880520 ; GB 1989-24696 19891102; WO 1995-EP622 19950221**
REP 5.Jnl.Ref; EP 122036; EP 257915; FR 2081353; GB 2176105; 1.Jnl.Ref
IC **A61K009-16**; A61K045-08
ICM A61K009-107; **A61K009-16**
ICS **A61K009-12**; **A61K009-14**; A61K009-18; **A61K009-50**; **A61K009-72**; A61K038-00; A61K038-27; A61K038-28; A61K039-00; A61K045-08; A61K047-30
AB WO 8809163 A UPAB: 19930923
Drug delivery systems comprise several **microspheres** contg. a drug and a **surfactant** (I) capable of enhancing the uptake of the drug. Pref. the **microspheres** have a partile size of 10-100 **microns**. They may have carrier selected from starch, starch derivs., gelatin, albumin, collagen, dextran and dextran derivs. The carrier may be crosslinked. (I) is pref. lysophosphatidylcholine (LPC), but may also be of nonionic-or biological-**surfactant**. The

microspheres may also contain other absorption enhancers, mucolytic agents and/or enzyme inhibitors.

USE/ADVANTAGE - Esp. useful for transmucosal (esp. intranasal, but also intravaginal or intraocular) admin. of high-mol. wt. substances, e.g. vaccines or polypeptides with a mol. wt. of 1000-300,000 (esp. insuli or growth hormone). Inclusion of (I) increases transmucosal absorption of the drug.

0/9

FS CPI
FA AB; DCN
MC CPI: B02-V02; B04-B02D4; B04-C01; B12-M02F; B12-M09
ABEQ GB 2231495 B UPAB: 19930923

A drug delivery system for transmucosal delivery including a plurality of **microspheres**, (i) formed of a biocompatible material, (ii) containing an active drug and (iii) including an adjuvant material associated with each **microsphere** which adjuvant material has the property of enhancing the uptake of the active drug across a mucosal membrane, wherein the said biocompatible material may be the said active drug.

ABEQ EP 391896 B UPAB: 19940418

A drug-delivery system for transmucosal delivery including a plurality of **microsphere** particles containing an active drug and including a material associated with each particle which material has the property of increasing the bioavailability of the active drug across a mucosal membrane.

Dwg.0/9

ABEQ US 5690954 A UPAB: 19980112

Drug delivery systems comprise several **microspheres** contg. a drug and a **surfactant** (I) capable of enhancing the uptake of the drug. Pref. the **microspheres** have a partile size of 10-100 **microns**. They may have carrier selected from starch, starch derivs., gelatin, albumin, collagen, dextran and dextran derivs. The carrier may be crosslinked. (I) is pref. lysophosphatidylcholine (LPC), but may also be of nonionic-or biological-**surfactant**. The **microspheres** may also contain other absorption enhancers, mucolytic agents and/or enzyme inhibitors.

USE/ADVANTAGE - Esp. useful for transmucosal (esp. intranasal, but also intravaginal or intraocular) admin. of high-mol. wt. substances, e.g. vaccines or polypeptides with a mol. wt. of 1000-300,000 (esp. insuli or growth hormone). Inclusion of (I) increases transmucosal absorption of the drug.

Dwg.0/17

L151 ANSWER 29 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1988-206601 [30] WPIX
CR 1992-358949 [44]
DNC C1988-092170
TI Soln. and suspension **aerosols** - contg. luteinising hormone releasing hormone analogues providing high bio-availability when given by inhalation.
DC B04
IN ADJEI, A L; JOHNSON, E S; KESTERSON, J W
PA (ABBO) ABBOTT LAB
CYC 16

PI	EP 275404	A	19880727 (198830)*	EN 9p		<--
	R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
	JP 63211237	A	19880902 (198841)			<--
	US 4851211	A	19890725 (198937)	6p		<--
	US 4897256	A	19900130 (199012)	6p		<--
	CA 1300009	C	19920505 (199223)		A61K037-43	<--
	EP 275404	B1	19930421 (199316)	EN 12p	A61K009-08	<--
	R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
	DE 3785570	G	19930527 (199322)		A61K009-08	<--

ES 2040727 T3 19931101 (199348) A61K009-08 <--
JP 2533586 B2 19960911 (199641) 6p A61K038-04
ADT EP 275404 A EP 1987-117226 19871123; JP 63211237 A JP 1987-298857 19871125; US 4851211 A US 1986-934874 19861125; US 4897256 A US 1987-114359 19871104; CA 1300009 C CA 1987-552274 19871119; EP 275404 B1 EP 1987-117226 19871123; DE 3785570 G DE 1987-3785570 19871123, EP 1987-117226 19871123; ES 2040727 T3 EP 1987-117226 19871123; JP 2533586 B2 JP 1987-298857 19871125
FDT DE 3785570 G Based on EP 275404; ES 2040727 T3 Based on EP 275404; JP 2533586 B2 Previous Publ. JP 63211237
PRAI **US 1986-934874 19861125; US 1987-114359 19871104**
REP 1.Jnl.Ref; EP 111841; FR 2205307; US 3560607; US 4476116
IC ICM A61K009-08; A61K037-43; A61K038-04
ICS A01N025-02; **A61K009-12**; **A61K009-72**; A61K047-12; A61K047-20
AB EP 275404 A UPAB: 19931116
Aerosol formulations contain (A) a luteinising hormone-releasing hormone (LHRH) analogue (I), a lipopholic counterion, water, ethanol and propellant or (B) (I), **surfactant**, solvent and propellant.
(I) is leuprolide acetate (Ia); the lipophilic ion is an alkyl (esp. decyl) sulphonic acid or its salt; and the **surfactant** (opt. present in (A)) is sorbitan monoleate (SMO). The propellant is dichlorodifluoromethane (DCDFM) and in (B) the solvent is trichlorofluoromethane (TCFM).
USE/ADVANTAGE - The lipophilic counterions are efficient solubilisers, giving soln. formulations (A) with relative bioavailability about 90% (relative to intravenous compsns.) when administered by inhalation. the suspension formulations (B) can be made by wet milling in a low b.pt. solvent, avoiding the losses and health hazards associated with usual **micronisation** procedures.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-B02D4; B07-A02; B07-D03; B10-A09B; B10-H02B; B12-G04; **B12-M01A**; B12-M09
ABEQ EP 275404 B UPAB: 19930923
A solution **aerosol** formulation of a LHRH analog comprising a LHRH analog; a lipophilic counter ion selected from an alkylsulphonic acid of from 5 to 12 carbon atoms, palmitic acid, dioctylsulphosuccinic acid, stearic acid, and salicyclic acid, or a salt thereof; water; ethyl alcohol; a **surfactant** selected from mono- or diglycerides, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene sorbitol esters, polyoxyethylene acids, polyoxythylene alcohols, and polyoxyethylene adducts; and a propellant.
0/0
ABEQ US 4851211 A UPAB: 19930923
New **aerosol** formulation comprises 0.001-15 (0.01-2) (1) mg/g LHRH analog (pref. leuprolide acetate); 0.05-10 (0.01-2) (0.2) mg/g lipophilic counter ion viz. 5-12 (10)C alkyl sulphonic acid or salt; 0.1-15 (3.5)% w/w water; 0.5-60 (0.5-50) (25)% w/w ethanol and q.s. (69% w/w propellant).
Pref. also 0.05-6 (1.3)% w/w **surfactant** (Na monooleate). Propellant is chlorofluorocarbon, pref. dichlorodifluoromethane.
ADVANTAGE - Allows admin. of LHRH analogs-leuprolide 5-ozo-L-Pro-L-His-L-Trp-L-Ser-L-Tyr-D -Leu-L-Leu-L-Arg-L-Pro-ethylamideacetate (I)
and related octadecapeptides by **aerosol** with almost 100% bioavailability. Previously admin. had to be p.e because of low G.I. absorption and enzymatic decomposition.
ABEQ US 4897256 A UPAB: 19930923
Aerosol compsns. comprise: (a) 0.01-5 wt.% LHRH analogue; (b) 0.05-10 wt.% **surfactant**; (c) 0.55 wt.% solvent and (d) 30-99 wt.% propellant.

In pref. compsn. (a) is leuprolide acetate, (b) is sorbitan trioleate, (c) is trichlorofluoromethane and (d) is dichlorodifluoromethane.

USE/ADVANTAGE - The compsn. give high bioavailability of (a) by inhalation while overcoming the hazards of prior art **aerosol** prodn.

L151 ANSWER 30 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1988-063906 [09] WPIX
TI **Microcapsule** pharmaceutical formulation - contg. a lipid-soluble **surfactant** to retard release of drug from **microcapsules**.
DC A96 B05 B07
IN BOYES, R N; GILLEY, R M; PLEDGER, K L; TICE, T R
PA (INNO-N) INNOVATA BIOMED LTD; (BOYE-I) BOYES R N
CYC 36
PI WO 8801165 A 19880225 (198809)* EN 26p <--
RW: AT BE CH DE FR GB IT LU NL OA SE
W: AT AU BB BG BR CH DE DK FI GB HU JP KP KR LK LU MC MG MW NL NO RO SD SE SU US
EP 257915 A 19880302 (198809) EN <--
R: ES GR
AU 8777549 A 19880308 (198821) <--
ZA 8705937 A 19880218 (198822) <--
NO 8801533 A 19880815 (198838) <--
PT 85521 A 19880817 (198838) <--
DK 8801959 A 19880608 (198841) <--
EP 318492 A 19890607 (198923) EN <--
R: AT BE CH DE FR GB IT LI LU NL SE
GB 2211413 A 19890705 (198927) <--
JP 01503534 W 19891130 (199003) <--
GB 2211413 B 19900321 (199012) <--
CA 1302258 C 19920602 (199228) A61K009-72 <--
EP 257915 B1 19930310 (199310) EN 20p A61K009-50 <--
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3784594 G 19930415 (199316) A61K009-50 <--
ES 2053549 T3 19940801 (199432) A61K009-50 <--
US 5384133 A 19950124 (199510) 9p A61K009-12 <--
NO 176784 B 19950220 (199512) A61K009-50 <--
DK 171221 B 19960805 (199637) A61K009-52
JP 2765700 B2 19980618 (199829) 12p A61K009-52
KR 9514440 B1 19951128 (199903) A61K009-50 <--
ADT WO 8801165 A WO 1987-GB566 19870811; EP 257915 A EP 1987-307115 19870811; ZA 8705937 A ZA 1987-5937 19870811; EP 318492 A EP 1987-905237 19870811; GB 2211413 A GB 1989-2288 19890202; JP 01503534 W JP 1987-504741 19870811; GB 2211413 B GB 1989-2288 19890202; CA 1302258 C CA 1987-544224 19870811; EP 257915 B1 EP 1987-307115 19870811; DE 3784594 G DE 1987-3784594 19870811, EP 1987-307115 19870811; ES 2053549 T3 EP 1987-307115 19870811; US 5384133 A WO 1987-GB566 19870811, Cont of US 1989-317452 19890403, Cont of US 1992-860854 19920327, US 1993-84747 19930629; NO 176784 B WO 1987-GB566 19870811, NO 1988-1533 19880408; DK 171221 B WO 1987-GB566 19870811, DK 1988-1959 19880411; JP 2765700 B2 JP 1987-504741 19870811, WO 1987-GB566 19870811; KR 9514440 B1 WO 1987-GB566 19870811, KR 1988-700383 19880411
FDT DE 3784594 G Based on EP 257915; ES 2053549 T3 Based on EP 257915; NO 176784 B Previous Publ. NO 8801533; DK 171221 B Previous Publ. DK 8801959; JP 2765700 B2 Previous Publ. JP 01503534, Based on WO 8801165
PRAI **GB 1986-19519 19860811; GB 1987-63 19870105 ; GB 1989-2288 19890202**
REP No-citns.; 2.Jnl.Ref; EP 140085; EP 158441; EP 38979; 1.Jnl.Ref
IC ICM **A61K009-12**; **A61K009-50**; A61K009-52; **A61K009-72**
ICS **A61K009-14**; A61K009-40; A61K047-22
AB WO 8801165 A UPAB: 19931119

A novel pharmaceutical formulation comprises (i) **microcapsules** which consists of a biocompatible polymeric wall material (I) encapsulating a drug and (ii) a lipid-soluble **surfactant** (II), which is mixed with the **microcapsules** or is incorporated within or coats the wall of the **microcapsules**.

Pref. (II) are sorbitan fatty acid esters, e.g. sorbitan trioleate. The drug may be a bronchodilating agent, such as a beta-adrenergic agonist, a xanthine, an anti-cholinergic agent, a calcium antagonist or a leukotriene or other anti-asthma drug such as corticosteroids, disodium chromoglycate or antihistamine when the formulation is used by inhalation. Alternatively, the formulation may be used by oral admin.

ADVANTAGE - The **surfactant** retards the release of the drug from the **microcapsules**. The rate of release of the drug can be controlled with respect to time.

Dwg.0/2

FS CPI
FA AB; DCN
MC CPI: A12-V01; A12-W05; B04-C02A2; B04-C03C; B07-A02; B12-A06; B12-D04; B12-E04; B12-F01C; B12-F05B; B12-G01; B12-G07; B12-K02; B12-M10B; B12-M11E
ABEQ EP 257915 B UPAB: 19930923
A pharmaceutical formulation suitable for inhalation, comprising: (i) **microcapsules** having an average diameter of from 0.1 to 10 um which consist essentially of a biocompatible biodegradable polymeric wall material encapsulating a drug, and (ii) a lipid-soluble **surfactant** which is mixed with the **microcapsules** or is incorporated within or costs the wall material of the **microcapsules**.
0/2
ABEQ GB 2211413 B UPAB: 19930923
A pharmaceutical formulation suitable for inhalation, comprising: (i) **microcapsules** having an average diameter of from 0.1 to 10 **microns** which consist essentially of a biocompatible bio-degradable polymeric wall material encapsulating a drug, and (ii) a lipid-soluble **surfactant** s which is mixed with the **microcapsules** or is incorporated within or coats the wall material of the **microcapsules**.
ABEQ US 5384133 A UPAB: 19950314
Pharmaceutical formulation suitable for inhalation comprises; (a) **microcapsules** of ave. dia. 0.1-10 **microns** comprising biodegradable, biocompatible wall forming polymer of mol.wt. greater than 10000 D encapsulating a drug (DG) and (b) 1-25 wt.% lipid-soluble **surfactant** comprising sorbitan trioleate, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, sorbitan monostearate, a polyoxomer or a fatty acid **surfactant**, incorporated into the polymer.

USE - Used for delivering antithrombotic, cardiovascular, anticonvulsant or chemotherapeutic drugs (for cancer treatment), bronchodilators esp. beta-adrenergic agonists, xanthines, anticholinergic agents, leukotrienes or antagonists (esp. salbutamol or terbutaline calcium) or other anti asthma drugs selected from corticosteroids, sodium cromoglycate and antihistamines.

ADVANTAGE - Prior art methods for controlling asthma had unpleasant side effects.

Dwg.0/2

L151 ANSWER 31 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1987-362627 [51] WPIX
DNC C1987-155323
TI **Aerosol** compsn. and pro-liposome prepn. - show high initial entrapment of active cpd. in membrane lipid with sustained release at site of application.
DC B05 B07
IN LEIGH, S

PA (PHAR-N) PHARES PHARM RES NV; (LEIG-I) LEIGH S; (PHAR-N) PHARES-PHARM RES NV

CYC 13

PI WO 8707502 A 19871217 (198751)* EN 32p <--
RW: AT BE CH DE FR GB IT LU NL SE
W: JP US
EP 309464 A 19890405 (198914) EN <--
R: AT BE CH DE FR GB IT LI LU NL SE
JP 01502979 W 19891012 (198947) <--
US 5141674 A 19920825 (199237) 15p A61K009-12 <--
EP 309464 B1 19921209 (199250) EN 25p A61K009-50 <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3783039 G 19930121 (199304) A61K009-50 <--
JP 2779165 B2 19980723 (199834) 13p A61K009-12 <--

ADT WO 8707502 A WO 1987-GB391 19870605; EP 309464 A EP 1987-903720 19870605; JP 01502979 W JP 1987-503432 19870605; US 5141674 A Cont of US 1985-709796 19850803, Cont of US 1988-171148 19880321, Cont of US 1988-282340 19881130, US 1991-719661 19910624; EP 309464 B1 EP 1987-903720 19870605, WO 1987-GB391 19870605; DE 3783039 G DE 1987-3783039 19870605, EP 1987-903720 19870605, WO 1987-GB391 19870605; JP 2779165 B2 JP 1987-503432 19870605, WO 1987-GB391 19870605

FDT US 5141674 A Cont of US 5004611; EP 309464 B1 Based on WO 8707502; DE 3783039 G Based on EP 309464, Based on WO 8707502; JP 2779165 B2 Previous Publ. JP 01502979, Based on WO 8707502

PRAI **GB 1986-13811 19860606**

REP EP 229561; EP 87993; US 3594476

IC ICM **A61K009-12; A61K009-50**
ICS A61K009-127; B01J013-02

AB WO 8707502 A UPAB: 19930922
Pro-liposomes may be prepd. by forming discrete particles of at least one membrane lipid (I) and one biologically active cpd. (II), the particles being free from solvent for (I) and (II) being present as discrete **micronised** particles. Pref. the compsn. is sprayed under pressure through a nozzle using a propellant. Also claimed is a pro-liposome compsn. comprising a volatile liq. propellant (III) in which a bilayer lipid is dispersed or dissolved, and (II) present in the lipid or (III) as dispersed **micronised** powder, the compsn. being free from other solvent for the drug.

Also new is a compsn. comprising discrete **micronised** particles consisting mainly of a solid carrier with a bilayer lipid and (II) in dispersion.

Propellants are CClF3, CCl2F2 and C2Cl2F2. (I) is pref. a natural or hydrogenated lecithin, a glycolipid, or a long chain dialkyl ammonium cpd. Active cpds. are salbutamol, terbutaline, orciprenaline, isoprenaline, reproterol, pirbuterol, butenoside, **beclomethasone dipropionate**, sodium chromoglycate, fenoterol, ipratropium, betamethasone valerate, rimiterol and ketotifen.

USE/ADVANTAGE - The compsn. may be used for treatment of asthma, bronchitis and hay fever and topically, to control psoriasis and inflammatory skin conditions, such as eczema. The compsn. and method of prepn. combine high initial entrapment of the active cpd. in the lipid with sustained release at the site of applicn. The **aerosol** type compsn. does not require solvents or water and gives more control over particle size with improved stability.

0/6

FS CPI

FA AB; DCN

MC CPI: B01-B02; B04-A01; B04-A06; B04-B01B; B06-A01; B06-B02; B07-D04; B07-D05; B10-B03B; B10-H02B; B10-H02F; B12-A07; B12-D02; B12-D07; B12-K02; B12-K06; B12-M11F

ABEQ EP 309464 B UPAB: 19930922
A composition comprising a membrane lipid together with a biologically active compound and which has the property of spontaneously forming

vesicles on contact with an excess of water, characterised in that: (a) the composition is a solid which comprises discrete **micronised** particles; (b) the biologically active compound is present in the form of discrete **micronised** particles; and (c) the composition is free from solvent for the biologically active compound.
0/6

ABEQ US 5141674 A UPAB: 19930922
A new method for prepn. of a pro-liposome compsn. comprises providing a membrane lipid, which on contact with water forms lipid bilayer vesicles contg. aq. space and dispersing in it **micronised** particles of drug using a solvent for the lipid which is a non-solvent for the drug.
Pref. the lipid is lecithin opt. hydrogenated, glycolipid or long-chain dialkyl ammonium cpd. or mixt. of above with a compatible lipophile. Pref. the drug is a bronchodilator, steroid, antibody, antihistamine, vasoconstrictor, or antiinflammatory (salbutamol, etc.). Pref. the drug is dispersed as 0.5 **micron** particles in the lipid.
Alternatively, pro-liposomes may be prepd. by dispersing the drug in the above vesicular lipid by forming discrete **micronised** particles in situ, pref. with a (swellable) carrier as major component (glucose or lactose). Solvent may be used, then evapd. off. Vesicles are formed by contacting the pro-liposomes with water, opt. in vivo. **Aerosol** pro-liposomes may be obtd. by introducing the **micronised** particles into an air stream.
ADVANTAGE - High initial entrapment and sustained release of drug.
0/6

L151 ANSWER 32 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1986-212033 [32] WPIX
DNC C1986-091292
TI **Aerosol** formulation contg. chloro-fluoro-carbon propellant and drug - with glycerol phosphatide to enhance dissolution of drug in propellant.
DC B07
IN BELL, A; FISCHER, F X; JINKS, P A
PA (JINK-I) JINKS P A; (RIKL) RIKER LAB INC
CYC 25
PI WO 8604233 A 19860731 (198632)* EN 21p <--
RW: AT BE CH DE FR GB IT LI LU NL SE
W: AU DK FI HU JP KR NO US
PT 81839 A 19860717 (198640) <--
AU 8653064 A 19860813 (198644) <--
ZA 8600045 A 19860908 (198648) <--
NO 8603683 A 19861201 (198703) <--
EP 209547 A 19870128 (198704) EN <--
R: AT BE CH DE FR GB IT LI LU NL SE
DD 241422 A 19861210 (198715) <--
FI 8603730 A 19860915 (198723) <--
JP 62501906 W 19870730 (198736) <--
HU 42938 T 19870928 (198743) <--
DK 8604403 A 19860915 (198745) <--
ES 8800037 A 19880101 (198809) <--
US 4814161 A 19890321 (198914) <--
CA 1264297 A 19900109 (199006) <--
EP 209547 B 19900912 (199037) <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3674098 G 19901018 (199043) <--
KR 8904690 B 19891125 (199044) <--
IL 77467 A 19901223 (199107) <--
NO 172727 B 19930524 (199326) A61K009-12 <--
FI 90014 B 19930915 (199341) A61K009-72 <--
JP 08011725 B2 19960207 (199610) 6p A61K009-12 <--
ADT WO 8604233 A WO 1986-GB1 19860102; ZA 8600045 A ZA 1986-45 19860103; EP

209547 A EP 1986-900606 19860102; JP 62501906 W JP 1986-500323 19860102; ES 8800037 A ES 1986-550891 19860115; US 4814161 A US 1986-915971 19861110; NO 172727 B WO 1986-GB1 19860102, NO 1986-3683 19860915; FI 90014 B WO 1986-GB1 19860102, FI 1986-3730 19860915; JP 08011725 B2 JP 1986-500323 19860102, WO 1986-GB1 19860102

FDT NO 172727 B Previous Publ. NO 8603683; FI 90014 B Previous Publ. FI 8603730; JP 08011725 B2 Based on JP 62501906, Based on WO 8604233

PRAI **GB 1985-1015 19850116**

REP DE 2802113; GB 2001334; GB 993702; US 3551558

IC A01N025-06; **A61K009-72**; A61K031-66; A61K047-00; C07F009-00; C09K003-30

ICM **A61K009-12**

ICS A01N025-06; **A61K009-72**; A61K031-66; A61K047-00; C07F009-00; C09K003-30

AB WO 8604233 A UPAB: 19930922

Aerosol formulation comprising a chlorofluorocarbon(s) propellent, a glycerol phosphatide (I) and a drug dissolved in the formulation is new.

(I) is esp. phosphatidylcholine, but phosphatidylethanolamine, -inositol or -serine, diphosphatidylglycerol or phosphatidic acid may also be used. (I) is used in purified form. A typical compsn. contains C13FC propellent and it is in the ratio to (I) of 100:0.01-20, esp. 100:0.01-3. Other propellents used include 12, 13, 21, 22, 113, 114, 115 and 500. The ratio of drug to (I) is 1-500:100, esp. 2-10:100. A small amt. of cosolvent may be included to enhance solubilisation. The drug is typically **beclomethasone dipropionate**, beta methasone **dipropionate**, acetate or valerate, salbutamol, atropine, prednisolone, formoterol or its HCl, hemisulphate or fumarate, diazepam, lorazepam, propranolol HCl, hydrocortisone, fluocinolone or triamcinolone acetonide, xylometazoline HCl, bitolerol mesylate or lacicortone.

USE/ADVANTAGE - The formulations are esp. suitable for topical, endopulmonary and nasal inhalation admin. of the drug. (I) causes enhanced or complete dissolution of certain drugs in the propellent, and even drugs that are nearly insoluble in the propellent alone can be solubilised.

0/0

FS CPI

FA AB

MC CPI: B01-B02; B04-B01B; B05-B01P; B10-H02B; **B12-M01A**; **B12-M01B**

ABEQ EP 209547 B UPAB: 19930922

An **aerosol** formulation which contains no dispersed phase comprising one or more chlorofluorocarbon **aerosol** propellents, glycerol phosphatide and a drug, the drug being dissolved in the composition.

ABEQ US 4814161 A UPAB: 19930922

New **aerosol** formulation comprises chlorofluorocarbon **aerosol** propellants, glycerol phosphatides and drug, normally insol. in propellant alone, but completely solubilised in phosphatide-contg. compsn. Pref. glycerol phosphatide is phosphatidylcholine (e.g. egg phosphatidyl choline) and opt. small amt. of co-solvent e.g. ethanol. Applicable to wide range of insol. drugs including **beclomethasone**, **dipropionate**, formoterol base diazepam, etc. Proportions are wt. ratios drug:glycerol phosphatide of 1-30:100 (2-10:100) and glycerol phosphatide:propellant 0.01-10:100 (0.01-3:100).

ADVANTAGE - Gives soluble formulations of insol. drugs with particle sizes 2-5 **microns** by augmenting solubility in propellant and by reverse micellar solubilisation.

L151 ANSWER 33 OF 38 WPIX (C) 2002 THOMSON DERWENT

AN 1986-182890 [28] WPIX

DNC C1986-078840

TI Stable **aerosol** formulation of **beclomethasone**

di propionate - is prepd. from solvate with 1-5C alcohol reduced in particle size.

DC B01 P34
PA (JINK-I) JINKS P A; (RIKL) RIKER LAB INC
CYC 20
PI WO 8603750 A 19860703 (198628)* EN 17p <--
RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK JP KR NO US
AU 8653087 A 19860722 (198639) <--
EP 205530 A 19861230 (198652) EN <--
R: BE CH DE FR GB IT LI NL SE
NO 8603321 A 19861117 (198701) <--
ES 8702136 A 19870316 (198716) <--
ZA 8509631 A 19870414 (198726) <--
DK 8603917 A 19860818 (198733) <--
JP 62501706 W 19870709 (198733) <--
EP 205530 B 19890222 (198908) EN <--
R: BE CH DE FR GB IT LI NL SE
US 4810488 A 19890307 (198912) <--
DE 3568334 G 19890330 (198914) <--
CA 1253806 A 19890509 (198923) <--
JP 07014880 B2 19950222 (199512) 5p A61K031-57 <--
ADT WO 8603750 A WO 1985-GB588 19851216; EP 205530 A EP 1986-900210 19851216; ES 8702136 A ES 1985-550076 19851218; ZA 8509631 A ZA 1985-9631 19851217; JP 62501706 W JP 1986-500413 19851216; US 4810488 A US 1986-902411 19860818; JP 07014880 B2 WO 1985-GB588 19851216, JP 1986-500413 19851216
FDT JP 07014880 B2 Based on JP 62501706, Based on WO 8603750
PRAI **GB 1984-32063 19841219**
REP DE 3018550; EP 393369; GB 1429184; GB 2107715; EP 39369
IC **A61K009-72**; A61K031-57; A61L009-04; C07J005-00; C09K000-00
ICM A61K031-57
ICS A61K047-10; A61L009-04; C09K000-00
ICA A61K009-12; A61K009-72; C07J005-00
AB WO 8603750 A UPAB: 19950322
Prepn. of a stable **aerosol** formulation of **beclomethasone dipropionate** (I) comprises contacting (I) with a 1-5C alcohol to form a **crystalline** solvate, which material has particle size reduced to less than 10 **microns**, and then dispersing in a compsn. contg. chlorofluorocarbon propellants.

Aerosol formulation of (I), opt. in the presence of a dispersing agent, suspended in an **aerosol** propellent, in which (I) is in the form of a **crystalline** solvate with a 1-5C alcohol, is also claimed.

USE/ADVANTAGE - The article size of (I) is such as to permit inhalation into the human bronchial system. The formulation exhibits a better thermal stability than compsns. employing solvates with ethyl actate. The stabilisation is simple and effective. (I) is an antiinflammatory agent.

0/7
Dwg.0/7
FS CPI GMPI
FA AB
MC CPI: B01-B02; B12-D07; **B12-M01A**; B12-M06
ABEQ EP 205530 B UPAB: 19930922
A method for preparing a stable **aerosol** formulation of **beclomethasone dipropionate** in which **beclomethasone dipropionate** is contacted with an alcohol contg. 1 to 5 carbon atoms to form a **crystalline** solvate therewith, the **crystalline** material so formed being reduced to a particle size below 10 **microns** and thereafter dispersed in a composition comprising chlorofluorocarbon propellents.
ABEQ US 4810488 A UPAB: 19930922
New method for prepn. stable **aerosol** formulation of

beclomethasone dipropionate comprises contacting it with 1-5C alcohol to form **crystalline** solvate which is ground to particle size below 10 **microns**, pref. 2-5 **microns** then dispersed in compsn. contg. chlorofluorocarbon propellants. Pref. alcohols are monohydric alkanols or alkenols, esp. isopropyl alcohol.

ADVANTAGE - Stable small **crystals** of steroid are prod. which can almost entirely be taken up by bronchial system, without growth of large **aerosol** complex **crystals**.

L151 ANSWER 34 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1986-056930 [09] WPIX
DNC C1986-024105
TI New di isopropyl ether solvates of **beclomethasone** 17, 21-**di propionate** - which are bulk-stable and have use in **aerosol** formulations for treatment of asthmatic conditions.
DC B01 P34
IN HEGGIE, W; PAGE, P R R
PA (HOVI-N) HOVIONE INT LTD; (PAGE-I) PAGE P R
CYC 20
PI EP 172672 A 19860226 (198609)* EN 9p <--
R: AT BE CH DE FR GB IT LI LU NL SE
AU 8545305 A 19860130 (198612) <--
NO 8502948 A 19860217 (198614) <--
DK 8503364 A 19860126 (198623) <--
JP 61083197 A 19860426 (198623) <--
PT 80796 A 19860717 (198640) <--
ES 8704182 A 19870601 (198726) <--
EP 172672 B 19880107 (198802) EN <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3561321 G 19880211 (198807) <--
JP 01029199 B 19890608 (198927) <--
IL 75903 A 19891031 (199004) <--
US 4913892 A 19900403 (199019) <--
CA 1274503 A 19900925 (199044) <--
ADT EP 172672 A EP 1985-305303 19850725; JP 61083197 A JP 1985-163086 19850725; ES 8704182 A ES 1985-550595 19851231; US 4913892 A US 1985-758287 19850724
PRAI **PT 1984-78972 19840725; PT 1984-78982 19840725 ; PT 1985-80796 19850711**
REP EP 39369; GB 2107715; US 4044126
IC **A61K009-72**; A61K031-57; A61L009-04; C07B005-00; C07J001-00; C07J005-00; C07J009-00
AB EP 172672 A UPAB: 19930922
Di-isopropyl ether solvates of **beclomethasone** 17,21-**dipropionate** are new. They pref. contain 3-10 wt.% of the ether. They are pptd. by addn. of the ether to a soln. of the steroid in an organic solvent.

USE/ADVANTAGE - **Beclomethasone** 17,21-**dipropionate** is used in the treatment of asthmatic complaints, but **crystals** of the steroid in **aerosol** formulations are prone to **crystal** growth and/or agglomeration, and can clog the metering valve in the **aerosol** and are also too large to penetrate far enough into the bronchial system. The present solvates avoid these disadvantages because they are substantially bulk-stable in both non-**micronised** and **micronised** forms. **Aerosols** can contain the solvate and a propellant gas such as trichlorofluoromethane or dichlorodifluoromethane.
0/0
FS CPI GMPI
FA AB
MC CPI: B01-B02; B10-H01; B12-D02; B12-K02; **B12-M01A**
ABEQ EP 172672 B UPAB: 19930922
Process for the preparation of di-isopropyl ether solvates of

beclomethasone 17,21-**dipropionate**, characterised by the fact that **beclomethasone** 17,21-**dipropionate** is dissolved in an organic solvent and is precipitated by addition of di-isopropyl ether.

ABEQ US 4913892 A UPAB: 19930922
Prepn. of new di-isopropyl ether solvates of **beclomethasone** 17,21-**dipropionate** comprises dissolution of the unsolvated cpd. in organic solvent (pref. THF, chloroform, dichloromethane or ether), and pptn. by addn. of di-isopropyl ether. Solvents contain 3-10% wt. di-isopropy ether.
USE - Prod. may be **micronised**, pref. to 2-5 **microns**, for use as **aerosol** with tri- or di-chloro-fluoromethane propellant for treatment of asthma at dose e.g. 50-600 mcg day. Storage stable.

L151 ANSWER 35 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1985-129102 [22] WPIX
DNC C1985-056149
TI Medicament-contg. biodegradable **nano**-particles - produced by surface polymerisation in or removal of organic solvent from emulsion in which inner phase size is below one **micron**.
DC A96 B07
IN ROHDEWALD, P; SAMALIGY, M
PA (KRAU-I) KRAUSE H J
CYC 1
PI DE 3341001 A 19850523 (198522)* 13p <--
ADT DE 3341001 A DE 1983-3341001 19831112
PRAI **DE 1983-3341001 19831112**
IC **A61K009-14**
AB DE 3341001 A UPAB: 19930925
Nano-particles of biodegradable synthetic material, having a mean diameter below 1 **micron** and contg. not less than 3% of medicaments or other biologically **active** substances are novel. Pharmaceutical preparations of the above **nanoparticles**, intended for injection, as **aerosols**, or for oral, nasal, vaginal or rectal application, are also novel. Emulsions in which the particle size of the inner phase is below 1 **micron** are produced by strong shear force (e.g. ultrasound), then, with constant stirring, the particles are produced by (a) **surface**-polymerisation in the presence of water and/or bases or (b) removal of the solvent for the synthetic polymer.
ADVANTAGES - Both water-soluble and poorly soluble medicaments can be incorporated into the **nanoparticles**. The medicaments go into solution more slowly than free medicaments of comparable **crystal** size, thus ensuring that the active substances are not released until the **nanoparticles** have reached the target organ. Bioavailability of poorly soluble medicaments is high.
0/2
FS CPI
FA AB
MC CPI: A12-V01; B04-C03D; B12-M10; B12-M11

L151 ANSWER 36 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1983-41599K [18] WPIX
DNC C1983-040660
TI **Micronised beclomethasone di propionate** mono hydrate - useful for treating asthma by inhalation.
DC B01
IN HUNT, J H; PADFIELD, J M
PA (GLAX) GLAXO GROUP LTD
CYC 23
PI BE 894725 A 19830418 (198318)* 16p <--

GB 2107715	A	19830505	(198318)			<--
DE 3238569	A	19830505	(198319)			<--
FR 2514769	A	19830422	(198321)			<--
NL 8204013	A	19830516	(198323)			<--
SE 8205904	A	19830530	(198324)			<--
JP 58090599	A	19830530	(198327)			<--
DK 8204611	A	19830620	(198331)			<--
FI 8203561	A	19830630	(198332)			<--
ZA 8207601	A	19830822	(198347)			<--
PT 75692	A	19831116	(198349)			<--
AU 8289460	A	19840503	(198425)			<--
ES 8404374	A	19840716	(198438)			<--
CA 1189853	A	19850702	(198531)			<--
GB 2107715	B	19851113	(198546)			<--
CH 652134	A	19851031	(198547)			<--
SE 454356	B	19880425	(198819)			<--
KR 8900664	B	19890322	(198941)			<--
US 4866051	A	19890912	(198946)			<--
DE 3238569	C	19910131	(199105)			<--
IT 1196553	B	19881116	(199111)			<--
JP 04024358	B	19920424	(199221)	5p	C07J001-00	<--
DK 168389	B	19940321	(199415)		C07J005-00	<--

ADT GB 2107715 A GB 1982-29740 19821018; US 4866051 A US 1985-696427 19850130; JP 04024358 B JP 1982-181500 19821018; DK 168389 B DK 1982-4611 19821018

FDT JP 04024358 B Based on JP 58090599; DK 168389 B Previous Publ. DK 8204611

PRAI **GB 1981-31425 19811019; GB 1982-29740 19821018**

IC ICM C07J001-00; C07J005-00

ICS **A61K009-14**; A61K009-48; A61K031-57; C07C000-00; C07J007-00; C07J009-00

ICA A61K031-56

ICI A61K031:57;

AB BE 894725 A UPAB: 19930925

Beclomethasone dipropionate (I) monohydrate, contg. no water other than water of **crystallisation**, has at least 90 wt.% of its particles of effective size below 10, pref. 2-5, **micron**. (I) monohydrate is characterised by IR spectra and powder X-ray diffraction pattern presented in the specification. Also new are compsns. consisting of **micronised** (I) monohydrate and at least one powder vehicle or excipient, particularly lactose. Suitable unit does contain 10-1000, eps. 50-500. **microg** (I) and opt. also salbutamol or Na cromoglycate.

(I) is a known topical antiinflammatory. In **micronised** form it is suitable for treatment (by inhalation as **aerosols**) of asthma and when used as the monohydrate can be stored for long periods without growth of **crystals** to unacceptable size.

FS CPI

FA AB

MC CPI: B01-B02; B12-D02; B12-D07; B12-K02; **B12-M01**

ABEQ DE 3238569 C UPAB: 19930925

Beclometasondipropionate (9alpha-chloro-11 beta-hydroxy-16 beta-methyl-17 alpha, 21-dipropionyl-oxypregna-1, 4-diene - 3, 20-dione) monohydrate (I), contg. at least 90 wt.% particles with a dia. of less than 10 **microns**, is new.

(I) is combined with a pharmaceutically acceptable dry powder carrier, pref. lactose.

USE/ADVANTAGE - As an inhalation for the treatment of asthma. Unlike prepns. contg. larger particles, the prod does not undergo **crystallisation**.

ABEQ GB 2107715 B UPAB: 19930925

Beclomethasone dipropionate monohydrate for use in the preparation of a pharmaceutical dry powder inhalation composition said monohydrate being substantially free from water other than water of **crystallisation**, at least 90% by weight of the particles thereof

having an effective particle size below 10 **microns**.

ABEQ US 4866051 A UPAB: 19930925
New compsn. comprises dry powder of **micronized beclomethasone dipropionate** monohydrate and excipient, with 90+% particle size below 10(2-5)**microns**.
Dosage unit for powder inhalation cartridge has 10-1000(50-500)mg halomethasone-**dipropionate** and salbutamol or Na cromoglycate.
USE- New treatment of bronchial conditions, e.g. asthma.

L151 ANSWER 37 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1982-90286E [42] WPIX
TI Self-propelling, powder dispensing **aerosol** - comprising finely divided solid (pref. medicament) coated with perfluorinated **surfactant** and dispersed in halogenated propellant.
DC B07 G04
IN THIEL, C G
PA (MINN) MINNESOTA MINING CO; (RIKL) RIKER LAB INC
CYC 6
PI US 4352789 A 19821005 (198242)* 9p <--
DE 3230743 A 19840223 (198409) <--
GB 2125426 A 19840307 (198410) <--
FR 2531972 A 19840224 (198413) <--
GB 2125426 B 19870603 (198722) <--
DE 3230743 C2 19950309 (199514) 10p C09K003-30 <--
ADT DE 3230743 A DE 1982-3230743 19820818; GB 2125426 A GB 1982-23172 19820811; FR 2531972 A FR 1982-14403 19820820; DE 3230743 C2 DE 1982-3230743 19820818
PRAI **US 1980-131030 19800317**
IC A61K007-12; **A61K009-14**; A61K031-18; C09K003-30
ICM C09K003-30
ICS A61K007-12; **A61K009-12**; **A61K009-14**; A61K031-18; A61K031-21; A61K031-66
AB US 4352789 A UPAB: 19930915
Self-propelling, powder dispensing **aerosol** compsn. comprises (A) 0.001-20 wt.% of a finely divided solid material (I) having a dry coating of a perfluorinated **surface-active** dispersing agent (II) which constitutes 0.1-20 wt.% of the coated solid material (I), suspended in (B) a halogenated propellant in which (I) and (II) are insoluble.
Pref. (I) is a medicament chosen from antiallergic, analgesic, bronchodilator, antihistamine, antitissive, antianginal, antibiotic, antiinflammatory, hormonal and/or sulphonamide cpds., and has a particle size of less than 100, esp. less than 10 **microns** dia. Pref. (II) is chosen from perfluorinated sulphonamide alcohol phosphate esters and their salts; perfluorinated alcohol phosphate esters, their free acids and their salts; perfluorinated alkyl sulphonamide alkylene quat. ammonium salts; and/or N,N-bis(carboxy-substd. lower alkyl) perfluorinated alkyl sulphonamides and their salts. Pref. (I) constitutes up to 3 wt.% of the total cosn., and (II) constitutes 0.25-1.0 wt.% of (I).
The **aerosol** is for dispensing medicament (I) for inhalation therapy. It provides a very fine spray of powdered material in which the individual powder particles are very small and have no tendency to glue together. Also, perfluorinated propellants can be used, which are environmentally more desirable than chlorofluorinated propellants.
FS CPI
FA AB
MC CPI: B05-B01P; B10-A08; B12-D01; B12-D02; B12-D06; B12-D07; B12-K02; **B12-M01**; G04-B07
ABEQ GB 2125426 B UPAB: 19930915
A self-propelling, powder dispensing **aerosol** composition comprising a powder suspended in a halogenated propellant, which halogenated propellant has a boiling point below 25 deg.C at atmospheric pressure, characterised in that said powder is finely-divided solid

material coated with a dry coating of a perfluorinated **surface-active** dispersing agent, and said solid material and said perfluorinated **surface-active** dispersing agent are substantially insoluble in said halogenated propellant.

ABEQ DE 3230743 C UPAB: 19950412
Material for spraying as an **aerosol** comprises 0.001-20 wt.% finely powdered active agent; **surfactant** dispersant; and a halo hydrocarbon propellant that is a gas at 25 deg.C, 1 atmos. pressure.

The active agent powder has a dry coating of a perfluorinated dispersant (IV) that comprises 0.1-20 wt.% of the powder. The powder and (IV) are both insol. in the propellant. (IV) is a perfluorinated sulphonamide alcoholphosphate ester or its salt, a perfluorinated alcoholphosphate ester or salt, or the free acid, a peprfluorinated alkylsulphonamide-alkylene-quat. ammonium salt and/or an N,N-(carboxy-substd. lower alkyl) perfluorinated alkylsulphonamide or salt.

USE/ADVANTAGE - The **aerosol** contains an agent which is effective against allergy, cough, angina or inflammation, or the agent is an antibiotic, sulphonamide, hormone, antiinflammatory, bronchodilator, antihistamine or analgesic. The **aerosol** can be stably formed.
Dwg.0/0

L151 ANSWER 38 OF 38 WPIX (C) 2002 THOMSON DERWENT
AN 1981-55134D [30] WPIX
TI **Beclomethasone** ester solvates - useful in inhalation devices (PT 28.1.80).
DC B01
IN FINCKENOR, L E
PA (ESSE-N) ESSEX LAAKKEET OY; (SCHE) SCHERING CORP
CYC 18
PI ZA 8002601 A 19810316 (198130)* 21p <--
PT 71281 A 19801128 (198051) <--
EP 39369 A 19811111 (198147) EN <--
R: AT BE CH DE FR GB IT LI NL SE
DK 8001859 A 19811207 (198201) <--
FI 8001446 A 19811231 (198204) <--
JP 57012000 A 19820121 (198209) <--
HU 22625 T 19820628 (198229) <--
EP 39369 B 19830615 (198325) EN <--
R: AT BE CH DE FR GB IT LI NL SE
CA 1147652 A 19830607 (198326) <--
DE 3063750 G 19830721 (198331) <--
IL 59981 A 19830731 (198336) <--
PRAI **PT 1980-71281 19800521**
REP 1.Jnl.Ref; ES 465924; FR 2361900; GB 1429184
IC **A61K009-72**; A61K031-57; C07C000-00; C07J005-00; C07J007-00
AB ZA 8002601 A UPAB: 19930915
Beclomethasone dipropionate solvates (I) with 5-8C alkanes are new. Prepn. of **beclomethasone dipropionate** -CCl3F solvate (II) involves contacting (I) with CCl3F. The (I) may be used in **micronised** form to give **micronised** (II). The (II) may be prepd. in situ in an **aerosol** formulation in which the propellant is also CCl3F.

Solvates (I) are stable on storage and they can be prepd. simply without use of large vols. of solvating medium. They are esp. useful in the prepn. of (II), which is used in **aerosols** for treating chronic allergic asthma. The (II), esp. in **micronised** form, is obtd. more economically and simply than as described e.g. in GB 1429184, and the (II) retains the particle size of the **micronised** form in an **aerosol**. (Provisional Basic advised Week D21)
FS CPI
FA AB
MC CPI: B01-B02; B10-H02; B12-D02; B12-K02

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=> d his

     (FILE 'REGISTRY' ENTERED AT 07:08:28 ON 19 JUL 2002)
                DEL HIS
                E BECLOMETHASONE/CN
L1            1 S E12
L2           34 S 5534-09-8/CRN
L3            5 S (WATER OR ETHANOL OR TERT-BUTANOL OR HEXANE OR GLYCOL)/CN
L4            9 S (GUM ACACIA OR CHOLESTEROL OR TRAGACANTH OR STEARIC ACID OR C
L5            6 S (SODIUM DODECYL SULFATE OR CARBOXYMETHYL CELLULOSE CALCIUM OR
L6            1 S (CELLULOSE, CARBOXYMETHYL ETHER, CALCIUM SALT)/CN
L7            1 S 9004-65-3
L8           97 S 9004-65-3/CRN
L9            8 S L8 AND ?PHTHAL?/CNS
L10           1 S 88-99-3
L11           2 S 88-99-3/CRN AND L8
L12          10 S (MAGNESIUM ALUMINUM SILICATE OR TRIETHANOLAMINE OR POLYVINYL
L13           1 S 9002-89-5
                E SULFOSUCCINIC ACID/CN
                E SULFOSUCCINIC ACID, SODIUM/CN
                E SULFOSUCCINIC ACID/CN
L14           1 S E3
L15         689 S 5138-18-1/CRN AND NA/ELS
L16           9 S L15 AND 2/NC NOT IDS/CI
L17           4 S L16 AND C4H6O7S
L18           4 S L17 NOT PMS/CI
                E SUCRUSE/CN
                E SUCROSE/CN
L19           1 S E144
                E SUCROSE DISTEARIC ACID/CN
L20          21 S 57-11-4/CRN AND 57-50-1/CRN AND IDS/CI
L21           1 S L20 AND C48H90O13
L22          35 S L4-L7,L11-L14,L18,L21

     FILE 'HCAPLUS' ENTERED AT 07:32:41 ON 19 JUL 2002
                E AEROSOL/CT
                E E17+ALL
L23       16673 S E4
                E E26+ALL
L24        1598 S E4,E5
                E DROPS/CT
                E E3+ALL
L25       33830 S E10/BI
                E E15+ALL
L26        3116 S E5
                E E6
                E E4+ALL
L27         265 S E2
L28       57714 S ?AEROSOL?
                E ATOMIZER/CT
                E E4+ALL
L29        1258 S E1
                E E2+ALL
                E NEBULIZER/CT
                E E4+ALL
L30        1145 S E2,E3
                E INHALER/CT
                E E5+ALL
                E INHALANT/CT
                E E4_ALL
                E INHALANT/CT
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                E E4+ALL
L31          258 S E2
                E INHALANT/CT
                E E7+ALL
L32         1636 S E2
L33        15730 S INHALANT? OR INHALER? OR NEBULIZ? OR NEBULIS? OR NOSESPRAY? O
L34            9 S NOSEDROP?
L35        46539 S ?DROPLET?
L36       116493 S L23-L35
                E PARTICLE SIZE/CT
                E E3+ALL
L37        44450 S E3
                E E3+ALL
                E E15+ALL
L38         3270 S E1(L)(MICRO? OR NANO? OR ULTRAFIN?)
L39        16705 S E7/BI
L40         1578 S E387
L41          130 S E365
L42         8785 S E389
                E PARTICLE SIZE/CT
                E E4+ALL
L43        63550 S ?NANOPARTICLE? OR ?NANOPARTICULAT? OR ?MICROPARTICLE? OR ?MIC
L44         7812 S L36 AND L37-L43
                E DRUG DELIVERY SYSTEM/CT
L45         1028 S E5-E7
L46          869 S E105
L47         2791 S E110,E113
L48          168 S E120
L49         3042 S E121,E123,E124,E125
L50          897 S E144,E152,E153
L51          177 S E171
L52         1295 S E177
                E E3+ALL
                E E4+ALL
L53        48056 S E3
L54         6666 S E10,E13,E14,E16,E18,E35-E38,E133,E134,E137-E139,E142,E146,E14
L55          868 S L44 AND L45-L54
L56         1049 S L44 AND 63/SC
L57         1115 S L55,L56
L58           57 S L57 AND L1,L2
L59           51 S L57 AND BECLOMETHASONE DIPROPIONATE
L60           24 S L57 AND CORTICOSTEROID
L61           72 S L58-L60
L62          111 S L57 AND ?CRYS?
L63          216 S L57 AND (SURFACTANT OR SURFACE ACTIV? OR SURFACE(S)MODIF?)
L64          530 S L57 AND L35
L65          200 S L57 AND (GELATIN OR CASEIN OR GUM(S)ACACIA OR CHOLESTEROL OR
L66          227 S L57 AND (SIO2 OR SILICA OR SILICON DIOXIDE OR PHOSPHATE OR (N
L67          430 S L57 AND (TYLOXAPOL OR ?POLYMER? OR POLYOXAMINE OR DEXTRAN OR
L68            7 S L57 AND (PEO(S)PPO OR ETHYLENE OXIDE(S)PROPYLENE OXIDE OR ETH
L69          443 S L63-L68 AND (LIQUID OR L23 OR H2O OR WATER OR SAFFLOWER(S)OIL
L70           49 S L62 AND L69
L71           18 S L61 AND L69
L72           63 S L70,L71
L73          117 S L61,L72

     FILE 'REGISTRY' ENTERED AT 08:04:03 ON 19 JUL 2002
L74            1 S 25322-68-3

     FILE 'HCAPLUS' ENTERED AT 08:04:11 ON 19 JUL 2002
L75           72 S L74 AND L57
L76          175 S L75,L73
                E WOOD R/AU
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L77         272 S E3,E37
L78          23 S E57,E60,E61
                E DECASTRO L/AU
L79           4 S E3,E4
                E DE CASTRO L/AU
L80          13 S E3-E7
                E BOSCH H/AU
L81          86 S E3,E12,E13
L82           2 S E23
L83           5 S L77-L82 AND L57
L84           4 S L83 AND L76
L85           5 S L83,L84
L86          62 S L76 AND ?CRYS?
L87          63 S L76 AND (PY<=1995 OR PRY<=1995 OR AY<=1995)
L88          32 S L86 AND L87
L89          49 S L87 AND (MICRO? OR NANO? OR ULTRAFIN?)
L90          58 S L87 AND 63/SC
L91          50 S L90 AND L88,L89
L92          52 S L76 AND AEROSOL
L93          17 S L92 AND L87
L94          63 S L87,L93 AND L23-L73,L75-L93
L95          18 S L94 AND ?AEROSOL?
                SEL DN AN 10 1 2 9 12 17
L96          12 S L95 NOT E1-E16
L97          15 S L85,L96
L98          79 S L87-L94 NOT L95-L97
L99          13 S L98 AND AEROSOL?/TI,CW
                SEL DN AN 4 8 12
L100         10 S L99 NOT E17-E25
L101         25 S L97,L100
L102         66 S L98 NOT L99-L101
                SEL DN AN 2 49 12 26 30 33 35 57 60
L103          9 S L102 AND E26-E52
L104         34 S L101,L103
L105         17 S L104 AND (LIQUID OR L3 OR H2O OR WATER OR SAFFLOWER OR ETHANO
L106         19 S L104 AND (L1 OR L2 OR BECLOMETHASONE OR CORTICOSTEROID)
L107         14 S L104 AND ?CRYS?
L108         34 S L104 AND (?PARTICULAT? OR ?PARTICLE OR ?PARTICLES OR ?CAPSUL?
L109         10 S L104 AND L35
L110         11 S L104 AND (GELATIN OR CASEIN OR ACACIA OR CHOLESTEROL OR TRAGA
L111         17 S L104 AND (PEG OR PPG OR ?PROPYLENEGLYCOL OR ?PROPYLENE GLYCOL
L112          2 S L104 AND (SLS OR SODIUM LAURYL SULFATE OR SUCROSE?)
L113         22 S L109-L112
L114         34 S L108-L113

     FILE 'HCAPLUS' ENTERED AT 08:34:31 ON 19 JUL 2002
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:35:07 ON 19 JUL 2002
L115         11 S E53-E63

     FILE 'REGISTRY' ENTERED AT 08:35:13 ON 19 JUL 2002

     FILE 'WPIX' ENTERED AT 08:35:30 ON 19 JUL 2002
                E WOOD R/AU
L116        115 S E3,E25,E27
                E DECASTRO L/AU
L117          2 S E3
                E DE CASTRO L/AU
L118          5 S E3,E4
                E BOSCH H/AU
L119         39 S E3,E6
L120        156 S L116-L119
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L121      18476 S ?AEROSOL?
L122       8089 S (R011 OR R012)/M0,M1,M2,M3,M4,M5,M6 OR (B12-M01 OR B12-M01A O
L123          3 S L120 AND L121,L122
L124        651 S L121,L122 AND (A61K009-14 OR A61K009-16 OR A61K009-72)/IC,ICM
L125        100 S L121,L122 AND (A61K009-50 OR A61K009-51)/IC,ICM,ICS
L126          3 S L124,L125 AND L123

     FILE 'HCAPLUS' ENTERED AT 08:47:24 ON 19 JUL 2002
              SET SMARTSELECT ON
L127        SEL L85 1- PN APPS :      31 TERMS
              SET SMARTSELECT OFF

     FILE 'WPIX' ENTERED AT 08:47:29 ON 19 JUL 2002
L128          3 S L127
L129          3 S L126,L128
L130        693 S L124-L125
L131        413 S L130 AND (PY<=1995 OR PRY<=1995)
              E R06390+ALL/DCN
              E R21380+ALL/DCN
              E R01629+ALL/DCN
L132         49 S L131 AND (BECLOMETHASONE DIPROPIONATE OR 1629/DRN OR R01629/D
L133        142 S L131 AND (NANO? OR MICRO? OR ULTRAFINE? OR ULTRA FINE?)
L134          4 S L131 AND SURFACE(S)MODIF?
L135         27 S L131 AND BECLOMETHASON?(S)DIPROPIONAT?
L136         62 S L131 AND SURFACTANT
L137         22 S L131 AND SURFACE(S)ACTIV?
L138         48 S L133 AND L132,L134-L137
L139          3 S L134 NOT ARTIFICIAL BLOOD
L140          4 S L129,L139
L141          3 S L138 AND L140
L142         45 S L138 NOT L140,L141
              SEL DN AN 2 3 9 19 22 26 28 29 30 31 38
L143         34 S L142 NOT E1-E24
L144         38 S L140,L141,L143
L145         19 S L144 AND BECLOMET?
L146         18 S L145 AND (DIPROPIONATE OR DI PROPIONATE)
L147         19 S L145,L146
L148         20 S L129,L147
L149         18 S L144 NOT L148
L150          9 S L148,L149 AND ?CRYS?
L151         38 S L148-L150

     FILE 'WPIX' ENTERED AT 09:10:29 ON 19 JUL 2002
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